STIC Search Report
EIC 1700

STIC Database Tracking Number: 191790

TO: Ben Sackey **Location: REM 5B31** **Art Unit : 1626** **June 6, 2006** **Case Serial Number: 10/726091**	**From: Les Henderson** **Location: EIC 1700** **REMSEN 4B30** **Phone: 571/272-2538** **Leslie.Henderson@uspto.gov**

Search Notes

The eight references in CAOLD are syntheses for the product (pp. 85-96), but none of the references include the borates or the catalysts.

ACCESS DB # 141110

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: BEN SACKEY Examiner #: 73489 Date: 6/1/06

Art Unit: 1626 Phone Number: 2-0204 Serial Number: 10/726,091

Location (Bldg/Room#): REM 5B31 (Mailbox #): Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Reductive alkylation of Saturated Cyclic Amines

Inventors (please provide full names): McManus et al

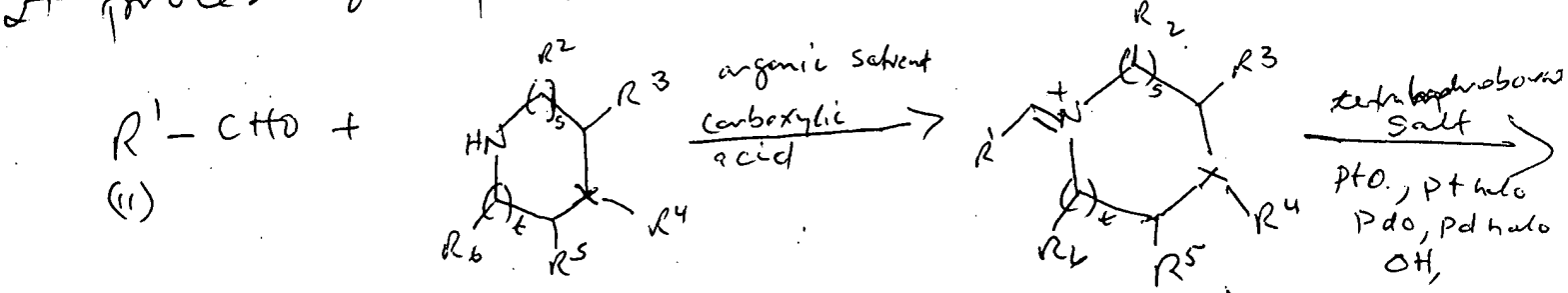
Earliest Priority Date: 12/11/02

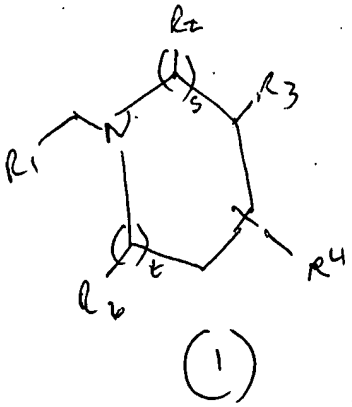
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

A process for preparing compound of formula (I)





(I)

X is CH or N.

The substituents are as defined in claim 1

Thanks

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=> d his ful

     (FILE 'HOME' ENTERED AT 09:08:14 ON 06 JUN 2006)

     FILE 'HCAPLUS' ENTERED AT 09:08:29 ON 06 JUN 2006
L1             1 SEA ABB=ON  PLU=ON  US20040116692/PN
                 D SCAN
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 09:08:58 ON 06 JUN 2006
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                 150323-38-9/BI OR 150378-17-9/BI OR 16940-66-2/BI OR
                 500-22-1/BI OR 58013-18-6/BI OR 64-19-7/BI OR 706791-28
                 -8/BI OR 706791-29-9/BI OR 83857-96-9/BI OR 92-54-6/BI)

L3             1 SEA ABB=ON  PLU=ON  706791-28-8/RN
                 D SCAN
L4             1 SEA ABB=ON  PLU=ON  58013-18-6/RN
                 D SCAN
L5             1 SEA ABB=ON  PLU=ON  150378-17-9/RN
                 D SCAN
L6             1 SEA ABB=ON  PLU=ON  706791-29-9/RN
                 D SCAN
L7             1 SEA ABB=ON  PLU=ON  16940-66-2/RN
                 D SCAN
L8             1 SEA ABB=ON  PLU=ON  1314-08-5/RN
                 D SCAN
L9             1 SEA ABB=ON  PLU=ON  11129-89-8/RN
                 D SCAN
L10            1 SEA ABB=ON  PLU=ON  500-22-1/RN
                 D SCAN
L11            1 SEA ABB=ON  PLU=ON  92-54-6/RN
                 D SCAN
L12            1 SEA ABB=ON  PLU=ON  83857-96-9/RN
                 D SCAN
L13            1 SEA ABB=ON  PLU=ON  150323-38-9/RN
                 D SCAN

     FILE 'CASREACT' ENTERED AT 09:23:02 ON 06 JUN 2006
                 D SAV
                 ACT SAC091/A
                ---------
L14              STR
L15          954 SEA SSS FUL L14 ( 10127 REACTIONS)

                ---------
                 ACT SAC091J/A
                ---------
L16              STR
L17 (        954)SEA SSS FUL L16 ( 10127 REACTIONS)
L18 (        338)SEA ABB=ON  PLU=ON  ((PT OR PD)(L)(O OR X))/ELS(L)2/ELC
                 .SUB
L19 (          9)SEA ABB=ON  PLU=ON  L17 AND L18/CAT
L20 (         82)SEA ABB=ON  PLU=ON  L17 AND 7440-05-3/CAT
L21 (          9)SEA ABB=ON  PLU=ON  L17 AND 1314-15-4/CAT
L22 (        783)SEA ABB=ON  PLU=ON  (M(L)B(L)H)/ELS(L)3/ELC.SUB
L23 (         69)SEA ABB=ON  PLU=ON  L17 AND L22/RRT
L24 (         85)SEA ABB=ON  PLU=ON  L19 OR L20 OR L21
L25           14 SEA ABB=ON  PLU=ON  L24 AND L23
                ---------
                 D QUE STAT L21
                 D QUE STAT L18
                 D QUE STAT L18
L26          349 SEA ABB=ON  PLU=ON  L15 AND ANY/CAT
L27            0 SEA ABB=ON  PLU=ON  L15 AND 1314-08-5/CAT
L28            0 SEA ABB=ON  PLU=ON  L15 AND 11129-89-8/CAT
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                D QUE L18

     FILE 'REGISTRY' ENTERED AT 09:37:59 ON 06 JUN 2006
L29          338 SEA ABB=ON  PLU=ON  ((PT OR PD)(L)(O OR X))/ELS(L)2/ELC
                 .SUB
                D QUE STAT L22
L30          783 SEA ABB=ON  PLU=ON  (M(L)B(L)H)/ELS(L)3/ELC.SUB
L31            1 SEA ABB=ON  PLU=ON  7440-05-3/RN
                D SCAN
L32            1 SEA ABB=ON  PLU=ON  1314-15-4/RN
                D SCAN

     FILE 'CASREACT' ENTERED AT 09:40:37 ON 06 JUN 2006
L33              STR L14
L34           25 SEA SUB=L15 SSS SAM L33 (   267 REACTIONS)
L35          416 SEA SUB=L15 SSS FUL L33 (  5643 REACTIONS)
                D SAV
                SAV L35 SAC091L/A
L36          164 SEA ABB=ON  PLU=ON  L35 AND ANY/CAT
L37            2 SEA ABB=ON  PLU=ON  L35 AND L29/CAT
                D SCAN
L38           35 SEA ABB=ON  PLU=ON  L35 AND L30/RRT
L39            6 SEA ABB=ON  PLU=ON  L38 AND (L29/CAT OR L32/CAT OR
                 L31/CAT OR L8/CAT OR L9/CAT)
L40           15 SEA ABB=ON  PLU=ON  L39 OR L25 OR L37

     FILE 'REGISTRY' ENTERED AT 09:50:29 ON 06 JUN 2006
                D SAV
                ACT SAC091C/A
               ---------
L41              SCR 1918 OR 2043
L42              SCR 1994
L43              SCR 1607
L44              STR
L45              SCR 1842
L46              SCR 1996
L47              SCR 1608
L48        13366 SEA SSS FUL L44 AND L47 AND L42 AND L43 NOT (L41 OR
                 L45 OR L46)
               ---------
                D QUE STAT

     FILE 'HCAPLUS' ENTERED AT 09:52:58 ON 06 JUN 2006
L49           15 SEA ABB=ON  PLU=ON  L40
L50         1519 SEA ABB=ON  PLU=ON  L48/P
L51            4 SEA ABB=ON  PLU=ON  L50 AND ((ALD OR ALDEHYDE?)/RACT)
L52         5866 SEA ABB=ON  PLU=ON  L29/CAT
L53         1337 SEA ABB=ON  PLU=ON  L8/CAT OR L9/CAT OR L32/CAT
L54        20456 SEA ABB=ON  PLU=ON  (PLATINUM OR PT OR PALLADIUM OR
                 PD)(A)(OXIDE OR O2 OR O4) OR PTO2 OR PTO4 OR PDO2 OR
                 PDO4
L55         1670 SEA ABB=ON  PLU=ON  (PLATINUM OR PT OR PALLADIUM OR
                 PD)(A)(HALIDE OR X2 OR X4) OR PTX2 OR PTX4 OR PDX2 OR
                 PDX4
L56         5472 SEA ABB=ON  PLU=ON  (L54 OR L55)(L)(CAT OR CATALYST?)
L57         5986 SEA ABB=ON  PLU=ON  L56 OR L53
L58            1 SEA ABB=ON  PLU=ON  L57 AND L50
L59         5659 SEA ABB=ON  PLU=ON  L30/RACT
L60            7 SEA ABB=ON  PLU=ON  L59 AND L50
L61            1 SEA ABB=ON  PLU=ON  L60 AND (L57 OR CAT OR CATAL?)
                D SCAN
L62           53 SEA ABB=ON  PLU=ON  L50 AND (CAT OR CATAL?)
L63         8811 SEA ABB=ON  PLU=ON  L7
L64         4367 SEA ABB=ON  PLU=ON  L7/RACT
L65        11683 SEA ABB=ON  PLU=ON  L30
L66         5659 SEA ABB=ON  PLU=ON  L30/RACT
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L67      166524 SEA ABB=ON  PLU=ON  L63 OR L65 OR ?BORATE OR BH4 OR
                NABH4 OR LIBH4 OR KBH4
L68           1 SEA ABB=ON  PLU=ON  L62 AND L67
                D SCAN
L69          34 SEA ABB=ON  PLU=ON  L50 AND L67
L70           1 SEA ABB=ON  PLU=ON  L69 AND (CAT OR CATAL?)
L71       15705 SEA ABB=ON  PLU=ON  L29
L72           1 SEA ABB=ON  PLU=ON  L71 AND L50
                D SCAN
L73           6 SEA ABB=ON  PLU=ON  L51 OR L58 OR L61 OR L68 OR L70 OR
                L72
L74        3911 SEA ABB=ON  PLU=ON  L48
L75           1 SEA ABB=ON  PLU=ON  L74 AND L57
L76           2 SEA ABB=ON  PLU=ON  L74 AND L71
                D SCAN
L77          56 SEA ABB=ON  PLU=ON  L74 AND L67
L78           4 SEA ABB=ON  PLU=ON  L77 AND (CAT OR CATAL?)
L79           1 SEA ABB=ON  PLU=ON  L3/P
L80           4 SEA ABB=ON  PLU=ON  L4/P
L81          55 SEA ABB=ON  PLU=ON  L5/P
L82           1 SEA ABB=ON  PLU=ON  L6/P
L83        1812 SEA ABB=ON  PLU=ON  L8
L84        1284 SEA ABB=ON  PLU=ON  L9
L85          58 SEA ABB=ON  PLU=ON  (L79 OR L80 OR L81 OR L82)
L86           1 SEA ABB=ON  PLU=ON  L85 AND (L83 OR L84)
L87           2 SEA ABB=ON  PLU=ON  L85 AND L63
L88           1 SEA ABB=ON  PLU=ON  L85 AND L71
L89           1 SEA ABB=ON  PLU=ON  L85 AND L57
L90           2 SEA ABB=ON  PLU=ON  L85 AND L65
                D SCAN
L91          11 SEA ABB=ON  PLU=ON  L73 OR (L75 OR L76) OR L78 OR (L86
                OR L87 OR L88 OR L89 OR L90)

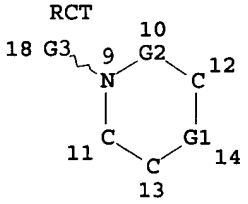
     FILE 'CAOLD' ENTERED AT 10:37:43 ON 06 JUN 2006
L92          51 SEA ABB=ON  PLU=ON  L48
L93         233 SEA ABB=ON  PLU=ON  L29
L94         175 SEA ABB=ON  PLU=ON  L30
L95           0 SEA ABB=ON  PLU=ON  L3
L96           0 SEA ABB=ON  PLU=ON  L4
L97           0 SEA ABB=ON  PLU=ON  L5
L98           0 SEA ABB=ON  PLU=ON  L6
L99           2 SEA ABB=ON  PLU=ON  L7
L100         32 SEA ABB=ON  PLU=ON  L8
L101          0 SEA ABB=ON  PLU=ON  L9
L102        175 SEA ABB=ON  PLU=ON  L99 OR L94
L103        233 SEA ABB=ON  PLU=ON  L93 OR L100
L104          0 SEA ABB=ON  PLU=ON  L92 AND L103
L105          0 SEA ABB=ON  PLU=ON  L92 AND L102
L106            QUE ABB=ON  PLU=ON  PRODUC? OR PROD# OR GENERAT? OR
                MANUF? OR MFR# OR CREAT? OR FORM## OR FORMING# OR
                FORMAT? OR MAKE# OR MADE# OR MAKIN# OR FABRICAT? OR
                SYNTHESI? OR PREPAR? OR PREP#
L107          8 SEA ABB=ON  PLU=ON  L92 AND L106
                D SCAN
                D QUE L67
L108       1960 SEA ABB=ON  PLU=ON  ?BORATE OR BH4 OR NABH4 OR LIBH4
                OR KBH4
L109          0 SEA ABB=ON  PLU=ON  L107 AND L108
L110          0 SEA ABB=ON  PLU=ON  L92 AND L108
L111          0 SEA ABB=ON  PLU=ON  L107 AND (CAT OR CATAL?)
                D L107 1-8 FHITSTR

     FILE 'HCAPLUS' ENTERED AT 10:49:42 ON 06 JUN 2006
L112         10 SEA ABB=ON  PLU=ON  L91 NOT L49

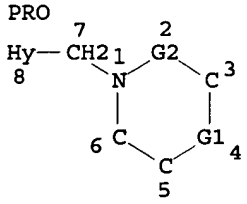
     FILE 'CASREACT' ENTERED AT 11:02:58 ON 06 JUN 2006
```

```
=> => d que stat l40
L8             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  1314-08-5/RN
L9             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  11129-89-8/RN
L14              STR
```

RCT



PRO



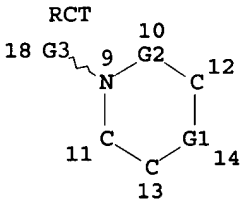

```
VAR G1=CH/N
REP G2=(0-1) C
VAR G3=H/16
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS UNS  AT   8
GGCAT   IS UNS  AT  15
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1 N  AT   8
ECOUNT  IS M1 N  AT  15

GRAPH ATTRIBUTES:
RSPEC   1   9
NUMBER OF NODES IS  17

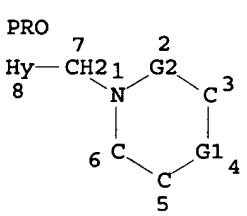
STEREO ATTRIBUTES: NONE

  ****MAPPINGS****
NOD SYM      ROL    NOD SYM      ROL
  1 N        PRO      9 N        RCT
  9 N        RCT      1 N        PRO
L15          954 SEA FILE=CASREACT SSS FUL L14 ( 10127 REACTIONS)
L16              STR
```

RCT



PRO




```
VAR G1=CH/N
REP G2=(0-1) C
VAR G3=H/16
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS UNS  AT   8
GGCAT   IS UNS  AT  15
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1 N  AT   8
ECOUNT  IS M1 N  AT  15

GRAPH ATTRIBUTES:
RSPEC   1   9
NUMBER OF NODES IS  17

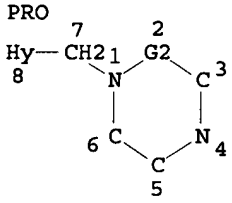
STEREO ATTRIBUTES: NONE
```

```
   ****MAPPINGS****
NOD SYM      ROL    NOD SYM      ROL
  1 N        PRO      9 N        RCT
  9 N        RCT      1 N        PRO
L17 (       954)SEA FILE=CASREACT SSS FUL L16 ( 10127 REACTIONS)
L18 (       338)SEA FILE=REGISTRY ABB=ON  PLU=ON  ((PT OR PD)(L)(O OR
                X))/ELS(L)2/ELC.SUB
L19 (         9)SEA FILE=CASREACT ABB=ON  PLU=ON  L17 AND L18/CAT
L20 (        82)SEA FILE=CASREACT ABB=ON  PLU=ON  L17 AND 7440-05-3/CAT

L21 (         9)SEA FILE=CASREACT ABB=ON  PLU=ON  L17 AND 1314-15-4/CAT

L22 (       783)SEA FILE=REGISTRY ABB=ON  PLU=ON  (M(L)B(L)H)/ELS(L)3/E
                LC.SUB
L23 (        69)SEA FILE=CASREACT ABB=ON  PLU=ON  L17 AND L22/RRT
L24 (        85)SEA FILE=CASREACT ABB=ON  PLU=ON  L19 OR L20 OR L21
L25          14 SEA FILE=CASREACT ABB=ON  PLU=ON  L24 AND L23
L29         338 SEA FILE=REGISTRY ABB=ON  PLU=ON  ((PT OR PD)(L)(O OR
                X))/ELS(L)2/ELC.SUB
L30         783 SEA FILE=REGISTRY ABB=ON  PLU=ON  (M(L)B(L)H)/ELS(L)3/E
                LC.SUB
L31           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  7440-05-3/RN
L32           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  1314-15-4/RN
L33             STR
```

PRO




```
REP G2=(0-1) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS UNS  AT   8
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1 N  AT   8

GRAPH ATTRIBUTES:
RSPEC   1
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
L35         416 SEA FILE=CASREACT SUB=L15 SSS FUL L33 (  5643 REACTIONS
                )
L37           2 SEA FILE=CASREACT ABB=ON  PLU=ON  L35 AND L29/CAT
L38          35 SEA FILE=CASREACT ABB=ON  PLU=ON  L35 AND L30/RRT
L39           6 SEA FILE=CASREACT ABB=ON  PLU=ON  L38 AND (L29/CAT OR
                L32/CAT OR L31/CAT OR L8/CAT OR L9/CAT)
L40          15 SEA FILE=CASREACT ABB=ON  PLU=ON  L39 OR L25 OR L37


=> d l40 1-15 fhit ibib abs ind

L40  ANSWER 1 OF 15  CASREACT  COPYRIGHT 2006 ACS on STN


RX(16) OF 621    ...K  ===>  AJ...
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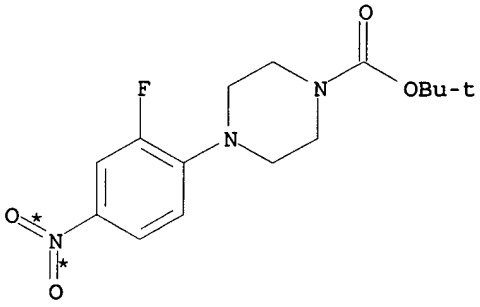
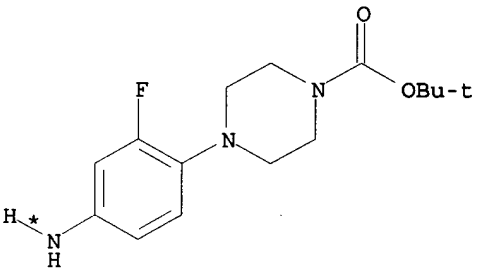


K

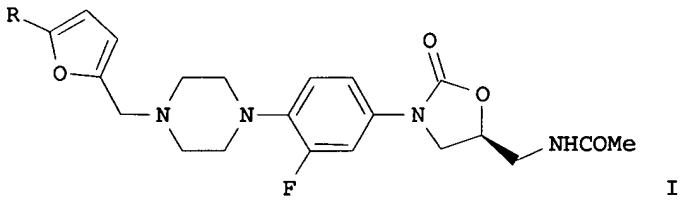
(16)



AJ

RX(16) RCT K 154590-34-8
RGT AK 1333-74-0 H2
PRO AJ 154590-35-9
CAT **7440-05-3** Pd
SOL 67-56-1 MeOH
CON room temperature, 55 psi
NTE high pressure

ACCESSION NUMBER: 143:386953 CASREACT
TITLE: Synthesis and SAR of novel oxazolidinones: Discovery of ranbezolid
AUTHOR(S): Das, Biswajit; Rudra, Sonali; Yadav, Ajay; Ray, Abhijit; Rao, A. V. S. Raja; Srinivas, A. S. S. V.; Soni, Ajay; Saini, Suman; Shukla, Shalini; Pandya, Manisha; Bhateja, Pragya; Malhotra, Sunita; Mathur, Tarun; Arora, S. K.; Rattan, Ashok; Mehta, Anita
CORPORATE SOURCE: Department of Medicinal Chemistry, Ranbaxy Research Laboratory, Gurgaon, 122001, India
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(19), 4261-4267
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Novel oxazolidinones, e.g. I (R = H, CHO, CO2H, HON:CH, CN, Cl, etc.), containing a number of substituted five-membered heterocycles attached to the piperazinyl-phenyl-oxazolidinone core of eperezolid, were synthesized. Further, the piperazine ring of the core was replaced by other diamino-heterocycles. These modifications led to several compds. with potent activity against a spectrum of resistant and susceptible Gram-pos. organisms, along with the identification of ranbezolid I (R = O2N) (RBx 7644) as a clin. candidate.

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 10

ST oxazolidinone piperazinylphenyl piperidinylphenyl prepn antibacterial; ranbezolid prepn antibacterial

IT Structure-activity relationship
(bactericidal; preparation and antibacterial activity of five-membered heterocycle-containing (homo)piperazinylphenyl- and piperidinylphenyl-substituted oxazolidinones)

IT Antibacterial agents
Infection
(preparation and antibacterial activity of five-membered heterocycle-containing (homo)piperazinylphenyl- and piperidinylphenyl-substituted oxazolidinones)

IT 392659-24-4P 548762-73-8P 548762-76-1P 866539-30-2P
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antibacterial activity of five-membered heterocycle-containing (homo)piperazinylphenyl- and piperidinylphenyl-substituted oxazolidinones)

IT 392659-25-5P 392659-31-3P 392659-33-5P 392659-39-1P
392659-46-0P 392659-49-3P 392659-58-4P 392659-63-1P
392659-73-3P 392659-86-8P 392659-87-9P 548762-75-0P
866539-20-0P 866539-21-1P 866539-22-2P 866539-23-3P
866539-24-4P 866539-25-5P 866539-26-6P 866539-27-7P
866539-28-8P 866539-29-9P 866539-31-3P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antibacterial activity of five-membered heterocycle-containing (homo)piperazinylphenyl- and piperidinylphenyl-substituted oxazolidinones)

IT 110-85-0, Piperazine, reactions 369-34-6, 1,2-Difluoro-4-nitrobenzene 505-66-8, Homopiperazine 617-88-9, 2-Chloromethylfuran 620-02-0, 5-Methyl-2-furancarboxaldehyde 698-63-5, 5-Nitro-2-furancarboxaldehyde, reactions 1623-88-7, 5-Chloromethyl-2-furaldehyde 2528-00-9, Ethyl 5-(chloromethyl)-2-furancarboxylate 4098-31-1, 2-(Chloromethyl)-5-nitrofuran 4521-33-9, 5-Nitro-2-thiophenecarboxaldehyde 6327-67-9, 5-Nitro-2-pyrrolecarboxaldehyde 18711-38-1, 1-Methyl-5-nitro-2-pyrrolecarboxaldehyde 21508-19-0, 5-Chloro-2-furancarboxaldehyde 21655-48-1, cis-2,6-Dimethylpiperazine 60456-26-0, (R)-Glycidyl butyrate 72918-24-2, 5-Nitro-3-furancarboxaldehyde 73874-95-0 113388-41-3 120737-59-9 134575-12-5 134575-17-0 172966-52-8 337914-79-1, 2-Bromo-5-chloromethylfuran

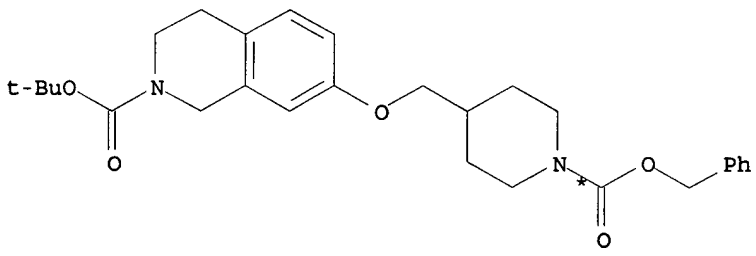
866538-96-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antibacterial activity of five-membered heterocycle-containing (homo)piperazinylphenyl- and piperidinylphenyl-substituted oxazolidinones)

IT 154590-33-7P 154590-34-8P 154590-35-9P 154590-36-0P
154590-62-2P 154590-63-3P 154590-64-4P 154590-65-5P
220220-24-6P 268209-15-0P 392659-38-0P 392659-98-2P
392659-99-3P 392660-00-3P 392660-01-4P 392660-02-5P
392660-03-6P 392660-04-7P 392660-05-8P 392660-06-9P
392660-08-1P 392660-09-2P 392660-10-5P 392660-11-6P
392660-12-7P 392660-13-8P 392660-14-9P 392660-15-0P
392660-16-1P 392660-18-3P 392660-19-4P 392660-20-7P
392660-21-8P 392660-22-9P 392660-23-0P 392660-24-1P
392660-25-2P 392660-26-3P 392660-27-4P 392660-28-5P
392660-29-6P 392660-30-9P 392660-31-0P 392660-32-1P
392660-33-2P 392660-34-3P 866538-93-4P 866538-94-5P
866538-95-6P 866538-97-8P 866538-98-9P 866538-99-0P
866539-00-6P 866539-01-7P 866539-02-8P 866539-03-9P
866539-04-0P 866539-05-1P 866539-06-2P 866539-07-3P
866539-08-4P 866539-09-5P 866539-10-8P 866539-11-9P
866539-12-0P 866539-13-1P 866539-14-2P 866539-15-3P
866539-16-4P 866539-17-5P 866539-18-6P 866539-19-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antibacterial activity of five-membered heterocycle-containing (homo)piperazinylphenyl- and piperidinylphenyl-substituted oxazolidinones)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(8) OF 465 ...AC ===> AE...



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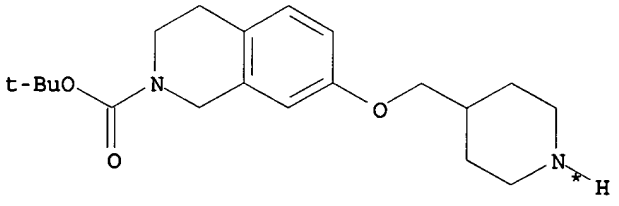
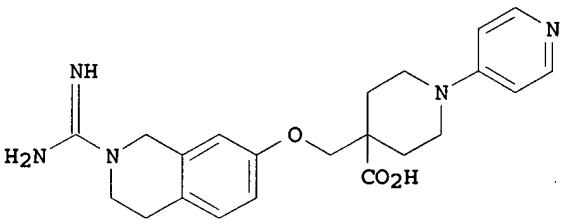


AE
YIELD 87%

RX(8) RCT AC 247132-98-5
RGT C 1333-74-0 H2
PRO AE 247132-99-6
CAT **7440-05-3** Pd
SOL 67-56-1 MeOH, 109-99-9 THF
CON 3 hours, room temperature

ACCESSION NUMBER: 143:59794 CASREACT
TITLE: Synthesis and Structure-Activity Relationships of Novel Selective Factor Xa Inhibitors with a Tetrahydroisoquinoline Ring
AUTHOR(S): Ueno, Hiroshi; Yokota, Katsuyuki; Hoshi, Jun-Ichi; Yasue, Katsutaka; Hayashi, Mikio; Hase, Yasunori; Uchida, Itsuo; Aisaka, Kazuo; Katoh, Susumu; Cho, Hidetsura
CORPORATE SOURCE: Central Pharmaceutical Research Institute, Japan Tobacco Inc., 1-1, Murasaki, Takatsuki, Osaka, 569-1125, Japan
SOURCE: Journal of Medicinal Chemistry (2005), 48(10), 3586-3604
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



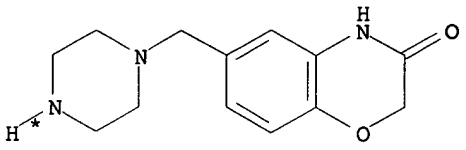
I

AB A series of novel 2,7-disubstituted tetrahydroisoquinoline derivs. were designed and synthesized. Among these derivs., compds. I.2HCl and I.MsOH exhibited potent inhibitory activity against factor Xa (FXa) and good selectivity with respect to other serine proteases (thrombin, plasmin, and trypsin). In addition, I.MsOH exhibited potent anti-FXa activity after i.v. and oral administration to cynomolgus monkeys, showed a dose-dependent antithrombotic effect at 0.1, 0.3, and 1 mg kg-1 h-1 in a rat model of venous thrombosis, and significantly reduced the size of brain infarction in a middle cerebral artery occlusion model at a dose of 0.1 mg kg-1 h-1. These results suggest that I.MsOH (JTV-803) is likely to be useful as both a venous and arterial antithrombotic agent.
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
ST tetrahydroisoquinoline prepn factor Xa inhibitor; isoquinoline tetrahydro prepn factor Xa inhibitor
IT Thrombosis
(arterial; preparation of 2,7-disubstituted tetrahydroisoquinoline derivs. as factor Xa inhibitors)
IT Anticoagulants
Structure-activity relationship
(preparation of 2,7-disubstituted tetrahydroisoquinoline derivs. as factor Xa inhibitors)
IT Thrombosis
(venous; preparation of 2,7-disubstituted tetrahydroisoquinoline

derivs. as factor Xa inhibitors)
IT 9002-05-5, Factor Xa
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 2,7-disubstituted tetrahydroisoquinoline derivs. as factor Xa inhibitors)
IT 247131-42-6P 247132-02-1P 854261-66-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2,7-disubstituted tetrahydroisoquinoline derivs. as factor Xa inhibitors)
IT 247130-99-0P 247131-05-1P 247131-11-9P 247131-14-2P
247131-44-8P 247131-54-0P 247131-55-1P 247131-60-8P
247131-79-9P 247131-95-9P 832088-72-9P 854261-58-8P
854261-60-2P 854261-62-4P 854261-63-5P 854261-64-6P
854261-65-7P 854261-67-9P 854261-68-0P 854261-69-1P
854261-70-4P 854261-71-5P 854261-72-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 2,7-disubstituted tetrahydroisoquinoline derivs. as factor Xa inhibitors)
IT 177-11-7, 1,4-Dioxa-8-azaspiro[4.5]decane 611-35-8, 4-Chloroquinoline 867-13-0 1126-09-6 1194-02-1 1822-51-1, 4-Picolyl chloride hydrochloride 2208-07-3 3678-63-5, 4-Chloro-2-methylpyridine 3934-20-1, 2,4-Dichloropyrimidine 3958-57-4 3958-60-9 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 5060-82-2 6836-19-7 6959-47-3, 2-Picolyl chloride hydrochloride 7379-35-3, 4-Chloropyridine hydrochloride 10314-98-4 14446-24-3 39989-39-4, 7-Methoxyisoquinoline 74291-57-9 76258-23-6 93913-86-1 114077-82-6, 4-Chloro-3-formylpyridine 121912-29-6 152120-54-2, 1H-Pyrazole-1-(N,N'-bis-tert-butoxycarbonyl)carboxamidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2,7-disubstituted tetrahydroisoquinoline derivs. as factor Xa inhibitors)
IT 22246-71-5P 90381-43-4P 110192-19-3P 122860-33-7P
126832-81-3P 130200-58-7P 130658-67-2P 135653-94-0P
142851-03-4P 158984-83-9P 159275-17-9P 188576-49-0P
213013-98-0P 247131-10-8P 247131-13-1P 247131-52-8P
247131-53-9P 247131-59-5P 247132-27-0P 247132-28-1P
247132-29-2P 247132-30-5P 247132-31-6P 247132-40-7P
247132-41-8P 247132-42-9P 247132-46-3P 247132-47-4P
247132-49-6P 247132-50-9P 247132-52-1P 247132-53-2P
247132-54-3P 247132-77-0P 247132-78-1P 247132-79-2P
247132-82-7P 247132-89-4P 247132-92-9P 247132-98-5P
247132-99-6P 247133-00-2P 247133-04-6P 247133-20-6P
247133-21-7P 247133-22-8P 247133-24-0P 247133-26-2P
247133-28-4P 247133-29-5P 247133-38-6P 247133-39-7P
247133-42-2P 247133-43-3P 247134-76-5P 374813-35-1P
832088-74-1P 854261-73-7P 854261-74-8P 854261-75-9P
854261-76-0P 854261-77-1P 854261-78-2P 854261-79-3P
854261-80-6P 854261-81-7P 854261-82-8P 854261-83-9P
854261-84-0P 854261-85-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2,7-disubstituted tetrahydroisoquinoline derivs. as factor Xa inhibitors)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

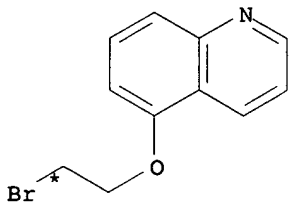
L40 ANSWER 3 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(21) OF 64 ...BM + BG ===> **BN**



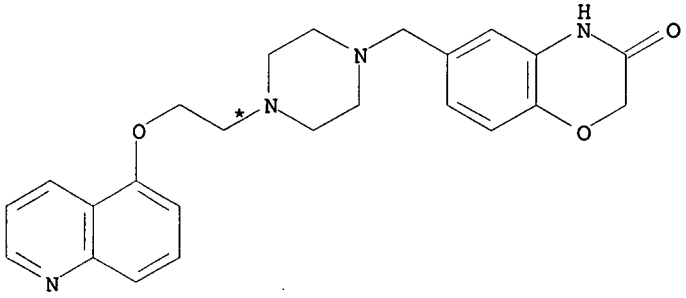
●2 HCl

BM



BG

(21) →



BN
YIELD 45%

RX(21) RCT BM 420786-49-8, BG 129717-28-8
RGT AX 7087-68-5 EtN(Pr-i)2
PRO BN **420785-66-6**
SOL 67-63-0 Me2CHOH
CON 48 hours, reflux

ACCESSION NUMBER: 142:253675 CASREACT
TITLE: 3,4-Dihydro-2H-benzoxazinones are 5-HT1A receptor antagonists with potent 5-HT reuptake inhibitory activity
AUTHOR(S): Atkinson, Peter J.; Bromidge, Steven M.; Duxon, Mark S.; Gaster, Laramie M.; Hadley, Michael S.; Hammond, Beverley; Johnson, Christopher N.; Middlemiss, Derek N.; North, Stephanie E.; Price, Gary W.; Rami, Harshad K.; Riley, Graham J.; Scott, Claire M.; Shaw, Tracey E.; Starr, Kathryn R.; Stemp, Geoffrey; Thewlis, Kevin M.; Thomas, David R.; Thompson, Mervyn; Vong, Antonio K. K.; Watson, Jeannette M.
CORPORATE SOURCE: Psychiatry Center of Excellence for Drug Discovery, GlaxoSmithKline, Essex, CM19 5AW, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(3), 737-741
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Starting from a high throughput screening hit, a series of 3,4-dihydro-2H-benzoxazinones has been identified with both high affinity for the 5-HT1A receptor and potent 5-HT reuptake inhibitory activity. The 5-(2-methyl)quinolinyloxy derivative

combined high 5-HT1A/1B/1D receptor affinities with low intrinsic activity and potent inhibition of the 5-HT reuptake site (pKi 8.2). This compound also had good oral bioavailability and brain penetration in the rat.

CC 1-3 (Pharmacology)
Section cross-reference(s): 28

ST dihydro benzoxazinone deriv 5HTA receptor antagonist 5HT reuptake structure

IT 5-HT reuptake inhibitors
Antidepressants
Anxiety
Anxiolytics
Human
Liver
(3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 5-HT agonists
(5-HT1A; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Mental and behavioral disorders
(depression; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dopamine transporter; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoamine; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(norepinephrine transporter; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Bioavailability
(oral; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Brain
(penetration; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin transporter; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT Neurotransmission
(serotoninergic; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT1A; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT1B; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT1D; 3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 50-67-9, 5-HT, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 420784-66-3P 420785-70-2P
RL: DMA (Drug mechanism of action); PAC (Pharmacological

activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 420784-63-0P 420784-64-1P 420784-75-4P 420784-79-8P
420784-84-5P 420784-86-7P 420784-88-9P 420785-33-7P
420785-34-8P 420785-66-6P 845887-36-7P 845887-37-8P
845887-38-9P 845887-39-0P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 845887-32-3
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

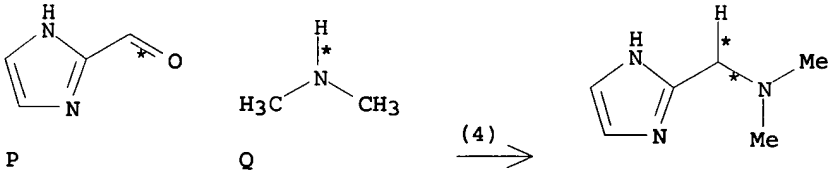
IT 96-32-2, Methyl bromoacetate 109-64-8, 1,3-Dibromopropane
611-35-8, 4-Chloroquinoline 2380-94-1, 4-Hydroxyindole
4606-65-9, 3-Piperidinemethanol 5082-74-6, 3-Pyrrolidinemethanol
5382-16-1, 4-Piperidinol 7652-26-8, 8-Allyloxyquinoline
13247-79-5 13985-43-8 19493-44-8, 1-Chloroisoquinoline
26690-80-2, N-Boc-ethanolamine 30934-97-5 35854-35-4
57260-71-6 119373-62-5 129717-28-8 150375-54-5 200195-15-9
420786-45-4 420786-67-0 420786-68-1 420786-70-5
845887-40-3 845887-42-5 845887-43-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

IT 70260-94-5P 420786-41-0P 420786-44-3P 420786-49-8P
420786-56-7P 583031-18-9P 754179-04-9P 845887-33-4P
845887-34-5P 845887-35-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(3,4-dihydro-2H-benzoxazinones preparation, 5-HT1A receptor antagonism and 5-HT reuptake inhibition)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(4) OF 497 P + Q ===> R...



P Q R
YIELD 76%

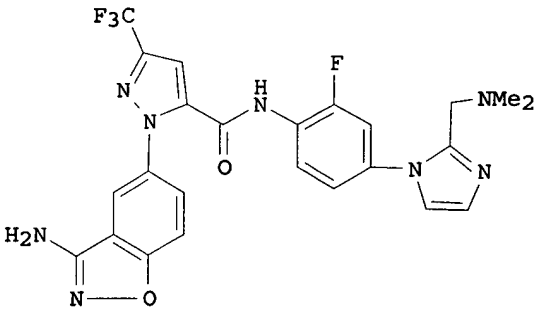
RX(4) RCT P 10111-08-7, Q 124-40-3

STAGE(1)
SOL 67-56-1 MeOH
CON 20 minutes, room temperature

STAGE(2)
RGT S **16940-66-2** NaBH4
CON SUBSTAGE(1) 45 minutes, room temperature -> 54 deg C
SUBSTAGE(2) 3 hours, 54 deg C -> 65 deg C
SUBSTAGE(3) 12 hours, 65 deg C -> room temperature

PRO R 54534-78-0
NTE safety(sodium borohydride should be added cautiously, foaming and an exothermic reaction occurs)

ACCESSION NUMBER: 142:219198 CASREACT
TITLE: Discovery of 1-(3'-Aminobenzisoxazol-5'-yl)-3-trifluoromethyl-N-[2-fluoro-4-[(2'-dimethylaminomethyl)imidazol-1-yl]phenyl]-1H-pyrazole-5-carboxyamide Hydrochloride (Razaxaban), a Highly Potent, Selective, and Orally Bioavailable Factor Xa Inhibitor
AUTHOR(S): Quan, Mimi L.; Lam, Patrick Y. S.; Han, Qi; Pinto, Donald J. P.; He, Ming Y.; Li, Renhua; Ellis, Christopher D.; Clark, Charles G.; Teleha, Christopher A.; Sun, Jung-Hui; Alexander, Richard S.; Bai, Steve; Luettgen, Joseph M.; Knabb, Robert M.; Wong, Pancras C.; Wexler, Ruth R.
CORPORATE SOURCE: Discovery Chemistry Pharmaceutical Research Institute, Bristol-Myers Squibb Co., Princeton, NJ, 08543-5400, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(6), 1729-1744
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Modification of a series of pyrazole factor Xa inhibitors to incorporate an aminobenzisoxazole as the P1 ligand resulted in compds. with improved selectivity for factor Xa relative to trypsin and plasma kallikrein. Further optimization of the P4 moiety led to compds. with enhanced permeability and reduced protein binding. The SAR and pharmacokinetic profile of this series of compds. is described. These efforts culminated in 1-(3'-aminobenzisoxazol-5'-yl)-3-trifluoromethyl-N-[2-fluoro-4-[(2'-dimethylaminomethyl)imidazol-1-yl]phenyl]-1H-pyrazole-5-carboxamide (I), a potent, selective, and orally bioavailable inhibitor of factor Xa. On the basis of its excellent in vitro potency and selectivity profile, high free fraction in human plasma, good oral bioavailability, and in vivo efficacy in antithrombotic models, the HCl salt of this compound was selected for clin. development as razaxaban (DPC 906, BMS-561389).

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST aminobenzisoxazolylimidazolylphenylpyrazolecarboxamide prepn
factor Xa inhibitor; razaxaban prepn factor Xa inhibitor
IT Human
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 218301-90-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(nod preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 9002-05-5, Factor Xa
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 536977-34-1P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 540510-38-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 218298-16-9P 218298-21-6P 218298-22-7P 218298-23-8P
218298-24-9P 218298-52-3P 218298-53-4P 218298-54-5P
218298-94-3P 218299-35-5P 218300-76-6P 405940-76-3P
540510-32-5P 540510-33-6P 540510-42-7P 540510-46-1P
754193-53-8P 754193-54-9P 754193-55-0P 754193-56-1P
754193-57-2P 754193-61-8P 754193-62-9P 754193-63-0P
754193-64-1P 754193-65-2P 754193-66-3P 754193-67-4P
754193-68-5P 754193-69-6P 754193-70-9P 754193-71-0P
754193-72-1P 754193-73-2P 754193-74-3P 754193-75-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 540510-41-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 110-91-8, Morpholine, reactions 326-90-9 350-46-9,
1-Fluoro-4-nitrobenzene 367-24-8, 4-Bromo-2-fluoroaniline
446-34-4, 2-Fluoro-4-methyl-1-nitrobenzene 446-35-5,
1,3-Difluoro-4-nitrobenzene 446-36-6, 5-Fluoro-2-nitrophenol
616-47-7 693-98-1, 2-Methyl-1H-imidazole 1072-62-4,
2-Ethyl-1H-imidazole 10111-08-7, 1H-Imidazole-2-carboxaldehyde
17417-09-3, 2-Fluoro-5-nitrobenzonitrile 29632-74-4,
2-Fluoro-4-iodoaniline 36947-68-9, 2-Isopropyl-1H-imidazole
209960-89-4 218631-45-9 754193-60-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)
IT 403-21-4P, 3-Fluoro-4-nitrobenzoic acid 3724-26-3P,
1H-Imidazole-2-methanol 50594-78-0P 53312-81-5P,
5-Amino-2-fluorobenzonitrile 54534-78-0P, 2-Dimethylaminomethyl-1H-imidazole 58610-69-8P 74852-81-6P 105494-69-7P
134485-96-4P 134485-97-5P 179552-68-2P 209958-42-9P
209960-29-2P 209960-58-7P 209960-59-8P 209960-85-0P
218301-47-4P 218301-62-3P 218301-68-9P 218301-72-5P
218301-73-6P 218301-74-7P 218301-83-8P 218301-84-9P
218301-85-0P 218301-86-1P 218301-88-3P 218301-89-4P

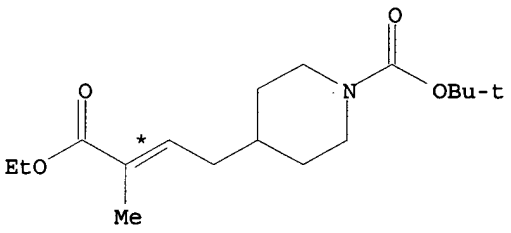
335275-99-5P 405940-74-1P 473927-49-0P 540510-44-9P
540510-45-0P 540510-47-2P 540510-48-3P 540510-49-4P
540510-50-7P 540510-51-8P 540510-52-9P 540510-54-1P
754193-45-8P 754193-46-9P 754193-47-0P 754193-48-1P
754193-49-2P 754193-50-5P 754193-51-6P 754193-52-7P
754193-58-3P 754193-59-4P 855869-57-7P 855869-58-8P
855869-60-2P 855869-81-7P 855869-83-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)

IT 546-88-3, N-Acetylhydroxylamine
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of razaxaban and related compds. as potent, selective, and orally bioavailable factor Xa inhibitors)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

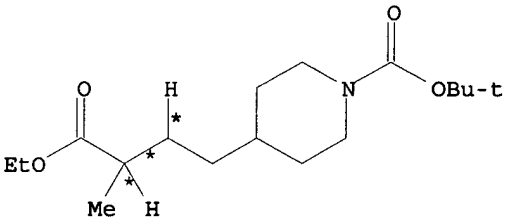
L40 ANSWER 5 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(2) OF 434 ...C ===> G...



C

(2) →

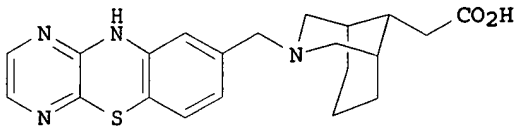


G
YIELD 87%

RX(2) RCT C 203662-10-6
RGT H 1333-74-0 H2
PRO G 203662-38-8
CAT **7440-05-3** Pd
SOL 64-17-5 EtOH
CON 2 days, room temperature

ACCESSION NUMBER: 141:207171 CASREACT
TITLE: Piperidine carboxylic acid derivatives of 10H-pyrazino[2,3-b][1,4]benzothiazine as orally-active adhesion molecule inhibitors
AUTHOR(S): Kaneko, Toshihiko; Clark, Richard S. J.; Ohi, Norihito; Ozaki, Fumihiro; Kawahara, Tetsuya;

Kamada, Atsushi; Okano, Kazuo; Yokohama, Hiromitsu; Ohkuro, Masayoshi; Muramoto, Kenzo; Takenaka, Osamu; Kobayashi, Seiichi
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co. Ltd., Tsukuba, 300-2635, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2004), 52(6), 675-687
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Novel piperidine carboxylic acid derivs. of 10H-pyrazino[2,3-b][1,4]benzothiazine were prepared and evaluated for their inhibitory activity on the upregulation of adhesion mols. such as intercellular adhesion mol.-1 (ICAM-1). Replacement of the methanesulfonyl group on the piperidine ring of previously prepared derivs. with a carboxylic acid-containing moiety resulted in a number of potent adhesion mol. inhibitors. Of these, (anti) [3-(10H-pyrazino[2,3-b][1,4]benzothiazin-8-yl)methyl-3-azabicyclo[3.3.1]non-9-yl]acetic acid (I, ER-49890), showed the most potent oral inhibitory activities against neutrophil migration in an interleukin-1 (IL-1) induced paw inflammation model using mice, and leukocyte accumulation in a carrageenan pleurisy model in the rat, and therapeutic effect on collagen-induced arthritis in rats.
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
ST pyrazino benzothiazine piperidine carboxylic acid prepn adhesion mol inhibitor; pyrazinobenzothiazine piperidinyl prepn adhesion mol inhibitor structure activity relationship
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD54; preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)
IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1); preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)
IT Pharmacokinetics
(adhesion mol. inhibitory activity and pharmacokinetic property of pyrazinobenzothiazine)
IT Neutrophil
(infiltration, suppression of; preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)
IT Pleura, disease
(pleurisy; preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)
IT Anti-inflammatory agents
Antiarthritics
Arthritis
Human

Structure-activity relationship
(preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)

IT Interleukin 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)

IT 203648-51-5
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(adhesion mol. inhibitory activity and pharmacokinetic property of pyrazinobenzothiazine)

IT 203646-55-3P 203646-98-4P 203647-29-4P 203650-26-4P
203650-42-4P 203650-45-7P 203650-60-6P 203650-69-5P
203650-75-3P 203650-81-1P 203650-93-5P 203650-94-6P
203651-09-6P 203651-12-1P 203651-14-3P 203651-31-4P
203651-58-5P 203651-62-1P 741730-06-3P 741730-07-4P
741730-08-5P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)

IT 100-39-0, Benzyl bromide 105-36-2, Ethyl bromoacetate
105-58-8, Diethyl carbonate 541-41-3, Ethyl chloroformate
867-13-0, Triethyl phosphonoacetate 1126-09-6, Ethyl isonipecotate 3612-20-2 3699-66-9, Triethyl 2-phosphonopropionate 4146-34-3 5130-24-5, Vinyl chloroformate
33577-16-1, FAMSO 34421-94-8, 4-Bromobenzaldehyde diethyl acetal
36635-61-7, 4-Methylphenylsulfonylmethyl isocyanide 50541-93-0
50893-53-3, 1-Chloroethyl chloroformate 56880-11-6 57988-58-6
59184-90-6, Ethyl (piperidin-4-yl)acetate 71879-55-5
94123-67-8 101966-77-2 109384-19-2 137076-22-3 142374-19-4
159635-49-1 203660-00-8 203660-02-0 203661-96-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)

IT 139362-30-4P 188863-87-8P 189889-45-0P 203646-54-2P
203646-60-0P 203648-08-2P 203649-09-6P 203649-23-4P
203649-42-7P 203649-48-3P 203649-53-0P 203649-54-1P
203649-58-5P 203649-61-0P 203649-68-7P 203649-81-4P
203650-01-5P 203650-06-0P 203660-03-1P 203660-04-2P
203660-05-3P 203660-10-0P 203660-11-1P 203661-62-5P
203661-63-6P 203661-69-2P 203662-10-6P 203662-22-0P
203662-31-1P 203662-38-8P 203662-42-4P 203662-66-2P
203662-68-4P 203662-69-5P 203662-78-6P 203662-82-2P
203662-84-4P 203663-44-9P 203663-45-0P 203663-57-4P
203663-59-6P 203664-61-3P 204011-62-1P 204015-91-8P
204015-93-0P 281235-04-9P 741729-82-8P 741729-83-9P
741729-85-1P 741729-86-2P 741729-87-3P 741729-88-4P
741729-89-5P 741729-90-8P 741729-91-9P 741729-92-0P
741729-93-1P 741729-94-2P 741729-95-3P 741729-96-4P
741729-97-5P 741729-98-6P 741729-99-7P 741730-00-7P
741730-01-8P 741730-02-9P 741730-03-0P 741730-04-1P
741730-05-2P 742097-86-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)

IT 128625-52-5, PyBop
RL: RGT (Reagent); RACT (Reactant or reagent)

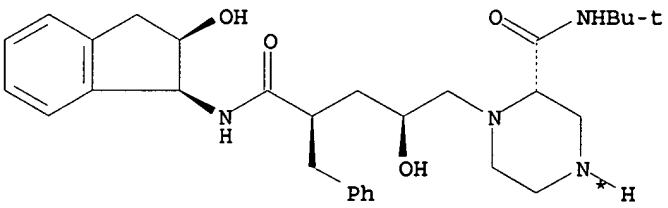
(preparation, adhesion mol. inhibitory activity, and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)

IT 204011-67-6P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, adhesion mol. inhibitory activity, pharmacokinetic property and structure-activity relationship of piperidine carboxylic acid derivs. of pyrazinobenzothiazine)

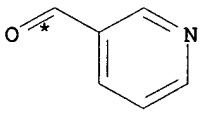
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(1) OF 6 **A** + B ===> **C**

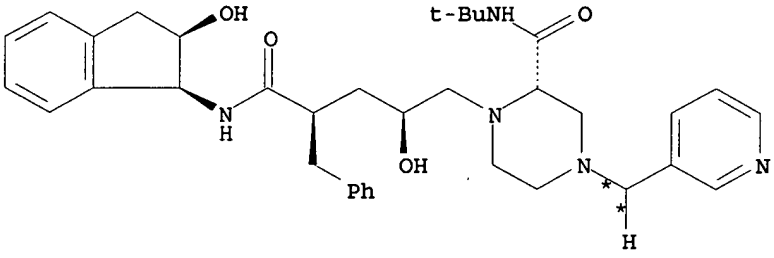


A



B

(1)



C
YIELD 92%

RX(1) RCT A **150323-38-9**, B 500-22-1

STAGE(1)
RGT D 64-19-7 AcOH
SOL 7732-18-5 Water, 109-99-9 THF
CON SUBSTAGE(1) room temperature
SUBSTAGE(2) 30 minutes, 20 deg C

STAGE(2)
RGT E **16940-66-2** NaBH4
CON SUBSTAGE(1) 30 minutes, 20 - 25 deg C
SUBSTAGE(2) 3 hours, 20 deg C

STAGE(3)
RGT F 7647-14-5 NaCl
SOL 7732-18-5 Water

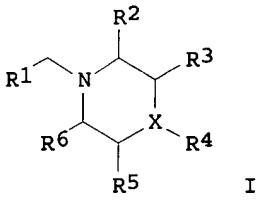
STAGE(4)
CAT **1314-15-4** PtO2
SOL 67-56-1 MeOH
CON SUBSTAGE(2) 1 hour
SUBSTAGE(3) 2 hours

PRO C **150378-17-9**
NTE mol. sieves were used

ACCESSION NUMBER: 141:54326 CASREACT
TITLE: Reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines
INVENTOR(S): Mcmanus, James W.; Kriel, Bryan G.; Stranberg, Michael
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004116692	A1	20040617	US 2003-726091	20031202
PRIORITY APPLN. INFO.:			US 2002-432570P	20021211

OTHER SOURCE(S): MARPAT 141:54326
GI



I

AB A process for the preparation of compds. of formula I (X = CH or N; R1 = heteroaryl; R2, R3, R5, and R6 = independently H, C1-6 alkyl or substituted alkyl, substituted or unsubstituted alkoxy, sulfoxide, OH, carboxy, sulfoxy, amide, or halogen; R4 = H, C1-20 alkyl) are prepared by the reductive alkylation of N-containing heteroaryl carbaldehyde using an alkylcarboxylic acid and a borohydride. Saturated cyclic amines are also reductively alkylated by adding an N-containing heteroaryl carbaldehyde and the amine to a tetrahydroborate salt-alkylcarboxylic acid-solvent admixt. and aging the resulting reaction mixture to obtain an alkylated product substantially free of borane complex. Thus, 1-phenylpiperazine, 3-pyridinecarboxaldehyde, and acetic acid were dissolved in THF and aged for 3 h at 55 °C, followed by the addition of NaBH4to give the borane which was treated with PdO in methanol to give 1-(phenyl)-4-((pyridin-3-yl)methyl)piperazine.

IC ICM C07D241-04
ICS C07D243-08
NCL 540575000
CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
ST reductive alkylation cyclic satd cyclic amine prepn

IT Amines, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cyclic; reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines)

IT Alkylation
(reductive; reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines)

IT 1314-08-5, Palladium oxide 11129-89-8, Platinum oxide
RL: CAT (Catalyst use); USES (Uses)
(reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines)

IT 706791-28-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines)

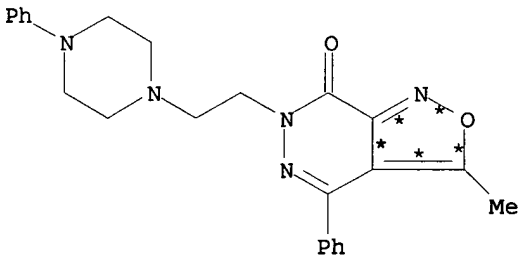
IT 58013-18-6P 150378-17-9P 706791-29-9P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines)

IT 92-54-6 500-22-1, 3-Pyridinecarboxaldehyde 83857-96-9 150323-38-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines)

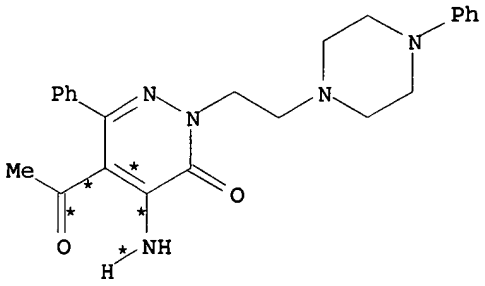
IT 64-19-7, Acetic acid, reactions 16940-66-2, Sodium tetrahydroborate
RL: RGT (Reagent); RACT (Reactant or reagent)
(reductive alkylation of saturated cyclic amines with heteroaryl carbaldehydes using a borohydride reducing agent to prepare substituted saturated cyclic amines)

L40 ANSWER 7 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(3) OF 147 ...G ===> H...



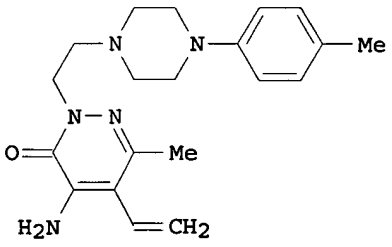
G (3) →



H
YIELD 72%

RX(3) RCT G 681828-67-1
RGT I 7803-57-8 N2H4-H2O
PRO H 681828-68-2
CAT **7440-05-3** Pd
SOL 64-17-5 EtOH
CON SUBSTAGE(1) 1 hour, reflux
SUBSTAGE(2) cooled

ACCESSION NUMBER: 140:357279 CASREACT
TITLE: 4-Amino-3(2H)-pyridazinones bearing arylpiperazinylalkyl groups and related compounds: synthesis and antinociceptive activity
AUTHOR(S): Dal Piaz, Vittorio; Vergelli, Claudia; Giovannoni, Maria Paola; Scheideler, Mark A.; Petrone, Giuseppe; Zaratin, Paola
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SOURCE: Farmaco (2003), 58(11), 1063-1071
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



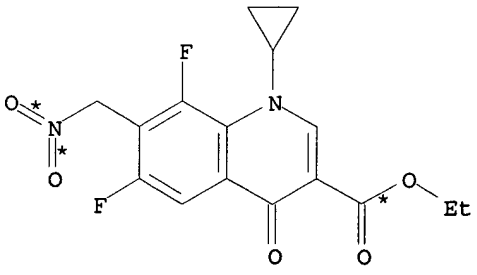
I

AB A series of 4-amino-3(2H)-pyridazinones substituted at position 2 with arylpiperazinylalkyl groups and analogs were synthesized and their antinociceptive effect was evaluated in the mouse abdominal constriction model. Preliminary SARs studies were performed. Several of the novel compds. dosed at 100 mg/kg s.c. significantly reduced the number of writhes induced by the noxious stimulus. Compound I showed 100% inhibition of writhes and was able to protect all the treated animals from the effect of the chemical stimulus. Subsequent dose-response studies revealed I to be almost 40-fold more potent than the structurally related Emorfazone.
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))

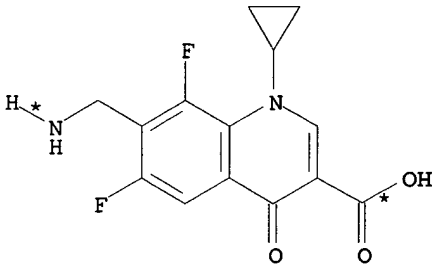
Section cross-reference(s): 1
ST aminopyridazinone arylpiperazinylalkyl prepn antinociceptive; structure activity arylpiperazinylalkylaminopyridazinone antinociceptive
IT Structure-activity relationship
(antinociceptive; of arylpiperazinylalkyl aminopyridazinones)
IT Analgesics
(preparation and antinociceptive effects of arylpiperazinylalkyl aminopyridazinones)
IT 681828-70-6P 681828-73-9P 681828-76-2P 681828-77-3P
681828-78-4P 681828-79-5P 681828-80-8P 681828-81-9P
681828-82-0P 681828-83-1P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antinociceptive effects of arylpiperazinylalkyl aminopyridazinones)
IT 92-54-6 106-93-4, 1,2-Dibromoethane 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 626-58-4
13339-01-0 15911-16-7 17334-68-8 17335-08-9 31252-42-3
35386-24-4 39512-50-0 39593-08-3 67980-67-0 681828-74-0
681829-14-1 681829-15-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antinociceptive effects of arylpiperazinylalkyl aminopyridazinones)
IT 51244-57-6P 681828-66-0P 681828-67-1P 681828-68-2P
681828-69-3P 681828-71-7P 681828-72-8P 681828-86-4P
681828-87-5P 681828-88-6P 681828-89-7P 681828-90-0P
681828-91-1P 681828-92-2P 681828-93-3P 681828-94-4P
681828-95-5P 681828-96-6P 681828-97-7P 681828-98-8P
681828-99-9P 681829-00-5P 681829-01-6P 681829-02-7P
681829-03-8P 681829-04-9P 681829-05-0P 681829-06-1P
681829-07-2P 681829-08-3P 681829-09-4P 681829-10-7P
681829-11-8P 681829-12-9P 681829-13-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antinociceptive effects of arylpiperazinylalkyl aminopyridazinones)
IT 681828-75-1P 681828-84-2P 681828-85-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antinociceptive effects of arylpiperazinylalkyl aminopyridazinones)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 8 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(1) OF 71 ...A ===> B



A (1) →



● HCl

B

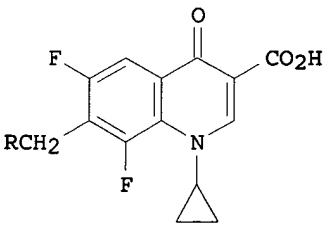
RX(1) RCT A 676586-71-3

STAGE(1)
RGT C 1333-74-0 H2
CAT **7440-05-3** Pd
SOL 64-17-5 EtOH

STAGE(2)
RGT D 64-19-7 AcOH, E 7647-01-0 HCl
SOL 7732-18-5 Water

PRO B 676586-55-3

ACCESSION NUMBER: 140:303500 CASREACT
TITLE: Synthesis and antibacterial activity of 7-(substituted)aminomethyl quinolones
AUTHOR(S): Zhang, Zhenfa; Zhou, Weicheng; Yu, Aizhen
CORPORATE SOURCE: Department of Biochemistry, Biomolecular Structure Center, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(2), 393-395
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of 7-(substituted)aminomethyl quinolones I (R = NH2, piperazinyl, 4-methylpiperazinyl, NHEt, NHPr, NHPr-i, cyclopropylamino, NHBu, NHPh, NHC6H4Cl-4, NHC6H4Cl-3, NHC6H4F-4, C6H4Me-4, 3-chloro-4-fluorophenyl, 3,4-dimethylphenyl, 4,6-dimethylpyridin-2-yl) was synthesized and evaluated for

antibacterial activity. Derivs. with (monoalkyl)aminomethyl substituent at C-7 displayed high in vitro activities comparable to lomefloxacin against gram-neg. organisms, whereas those bearing a [(substituted)phenyl]aminomethyl side chain at C-7 demonstrated good activities against gram-pos. organisms as potent as lomefloxacin and vancomycin.

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinolone substituted aminomethyl prepn antibacterial

IT Infection
(bacterial; preparation and antibacterial activity of substituted 7-aminomethylquinolones)

IT Structure-activity relationship
(bactericidal; preparation and antibacterial activity of substituted 7-aminomethylquinolones)

IT Antibacterial agents
(preparation and antibacterial activity of substituted 7-aminomethylquinolones)

IT 1404-90-6, Vancomycin 94242-53-2, 8-Fluorociprofloxacin 98079-51-7, Lomefloxacin
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation and antibacterial activity of substituted 7-aminomethylquinolones)

IT 676586-55-3P 676586-56-4P 676586-57-5P 676586-58-6P
676586-59-7P 676586-60-0P 676586-61-1P 676586-62-2P
676586-63-3P 676586-64-4P 676586-65-5P 676586-66-6P
676586-67-7P 676586-68-8P 676586-69-9P 676586-70-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antibacterial activity of substituted 7-aminomethylquinolones)

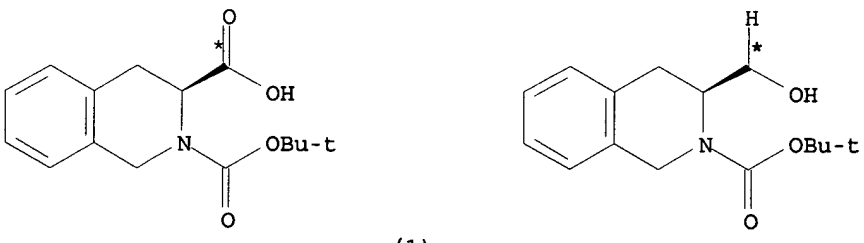
IT 94242-51-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antibacterial activity of substituted 7-aminomethylquinolones)

IT 676586-71-3P 676586-72-4P 676586-73-5P 676586-74-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antibacterial activity of substituted 7-aminomethylquinolones)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 9 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(1) OF 348 A ===> B...



A B

RX(1) RCT A 78879-20-6

STAGE(1)

RGT C 543-27-1 ClCO2Bu-i, D 109-02-4 N-Methylmorpholine
SOL 110-71-4 (CH2OMe)2
CON 5 minutes, 0 deg C

STAGE(2)
RGT E **16940-66-2** NaBH4
SOL 7732-18-5 Water
CON 15 minutes, 0 deg C

PRO B 183958-71-6

ACCESSION NUMBER: 139:127417 CASREACT
TITLE: New scaffolds in the development of Mu opioid-receptor ligands
AUTHOR(S): Page, Daniel; Nguyen, Natalie; Bernard, Sylvain; Coupal, Martin; Gosselin, Mylene; Lepage, Julie; Adam, Lynda; Brown, William
CORPORATE SOURCE: Department of Chemistry, AstraZeneca R&D Montreal, Saint-Laurent, QC, H4S 1Z9, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(9), 1585-1589
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new class of μ selective receptor antagonists has been developed using a combinatorial approach based on previously reported Dmt-Tic dipeptide ligands. Modified tetrahydroisoquinoline (Tiq) residues were reacted with different electrophiles in order to create novel mols. that would mimic the original dipeptide. A specific class of thioureas bearing basic pyrrolidine residues were shown to give good binding affinities. Further alkylation of the pyrrolidine ring with benzyl derivs. also proved to increase the μ binding affinity. In addition, it was demonstrated that μ binding was enhanced by the presence of polar groups around the benzyl ring having hydrogen-bonding character (donor/acceptor). This new class of ligands represents a novel scaffold in the development of opioid analogs.

CC 1-3 (Pharmacology)
Section cross-reference(s): 27

ST opioid receptor ligand structure activity relationship design

IT Combinatorial library
(new scaffolds in development of Mu opioid-receptor ligands)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(κ-opioid; new scaffolds in development of Mu opioid-receptor ligands)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(δ-opioid; new scaffolds in development of Mu opioid-receptor ligands)

IT Structure-activity relationship
(μ-opioid receptor-binding; new scaffolds in development of Mu opioid-receptor ligands)

IT Opioid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(μ-opioid; new scaffolds in development of Mu opioid-receptor ligands)

IT 568587-92-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(new scaffolds in development of Mu opioid-receptor ligands)

IT 568587-88-2P 568587-89-3P 568587-90-6P 568587-91-7P
568587-93-9P 568587-94-0P 568587-95-1P 568587-96-2P
568587-97-3P 568587-98-4P 568587-99-5P 568588-00-1P
568588-01-2P 568588-02-3P 568588-03-4P 568588-04-5P

568588-05-6P 568588-06-7P 568588-07-8P 568588-08-9P
568588-09-0P 568588-10-3P 568588-11-4P 568588-12-5P
568588-13-6P 568588-14-7P 568588-15-8P 568588-16-9P
568588-17-0P 568588-18-1P 568588-19-2P 568588-20-5P
568588-21-6P 568588-22-7P 568588-23-8P 568588-24-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(new scaffolds in development of Mu opioid-receptor ligands)

IT 66-99-9, 2-Formylnaphthalene 75-07-0, Acetaldehyde, reactions 75-36-5, Acetyl chloride 86-51-1, Benzaldehyde, 2,3-dimethoxy- 90-02-8, Benzaldehyde, 2-hydroxy-, reactions 100-83-4, Benzaldehyde, 3-hydroxy- 103-71-9, Benzene, isocyanato-, reactions 103-80-0, BenzeneAcetyl chloride 105-07-7, Benzonitrile, 4-formyl- 122-78-1, Benzeneacetaldehyde 122-85-0, Acetamide, n-(4-formylphenyl)- 123-08-0, Benzaldehyde, 4-hydroxy- 123-11-5, Benzaldehyde, 4-methoxy-, reactions 135-02-4, Benzaldehyde, 2-methoxy- 139-85-5, Benzaldehyde, 3,4-dihydroxy- 148-53-8, Benzaldehyde, 2-hydroxy-3-methoxy- 446-52-6, Benzaldehyde, 2-fluoro- 456-48-4, Benzaldehyde, 3-fluoro- 459-57-4, Benzaldehyde, 4-fluoro- 498-60-2, 3-Furanaldehyde 498-62-4, 3-Thiophenecarboxaldehyde 591-31-1, Benzaldehyde, 3-methoxy- 621-59-0, Benzaldehyde, 3-hydroxy-4-methoxy- 630-19-3, Propanal, 2,2-dimethyl- 1121-60-4, 3-Pyridinecarboxaldehyde 1609-86-5, Propane, 2-isocyanato-2-methyl- 7468-67-9, Benzonitrile, 2-formyl- 18278-34-7, Benzaldehyde, 4-hydroxy-2-methoxy- 24964-64-5, Benzonitrile, 3-formyl- 36810-87-4, Furan, tetrahydro-2-(isothiocyanatomethyl)- 78879-20-6 259537-92-3 639000-57-0 639001-07-3 639001-38-0 639001-41-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(new scaffolds in development of Mu opioid-receptor ligands)

IT 150417-17-7P 183958-71-6P 357339-32-3P 568587-84-8P 568587-85-9P 568587-86-0P 568587-87-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(new scaffolds in development of Mu opioid-receptor ligands)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 10 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(1) OF 1000 A ===> B...

A B

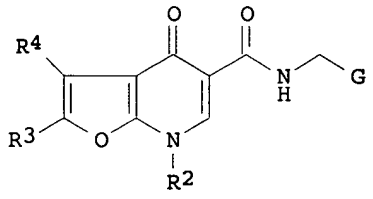
RX(1) RCT A 59-82-5
RGT C 1333-74-0 H2
PRO B 562100-62-3
CAT **7440-05-3** Pd
SOL 67-56-1 MeOH
CON 18 hours, room temperature, 40 psi

ACCESSION NUMBER: 139:117411 CASREACT
TITLE: Preparation of 4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide antiviral agents
INVENTOR(S): Cudahy, Michele M.; Shnute, Mark E.; Tanis,

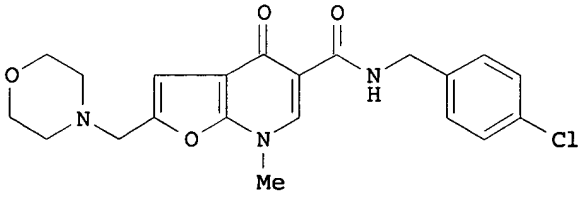
Steven P.; Perrault, William R.; Herrinton, Paul Matthew; Nair, Sajiv K.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059911	A2	20030724	WO 2003-US1041	20030114
WO 2003059911	A3	20040122		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2474127	AA	20030724	CA 2003-2474127	20030114
AU 2003219662	A1	20030730	AU 2003-219662	20030114
EP 1465895	A2	20041013	EP 2003-715931	20030114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003006904	A	20041123	BR 2003-6904	20030114
US 2004259907	A1	20041223	US 2003-345062	20030114
US 6878705	B2	20050412		
JP 2005521652	T2	20050721	JP 2003-560014	20030114
PRIORITY APPLN. INFO.:			US 2002-348718P	20020114
			WO 2003-US1041	20030114

OTHER SOURCE(S): MARPAT 139:117411
GI



I



II

AB Title compds. I [wherein G = Ph substituted with 1-5 R1 groups; R1 = Cl, Br, F, CN, (fluoro)alkyl, or NO2; R2 = H, R5, NR7R8, SO2R9, or OR9; R3 = H, halo, SOR6, SO2R6, COR6, CO2H, CO2R9, CN, OR12,

NR7R8, SR12, or (un)substituted heterocyclyl, aryl, or (cyclo)alkyl; R4 = H, halo, or (halo)alkyl; or R3 and R4 may form an (un)substituted carbocyclic or heterocyclic ring; R5 = (CH2CH2O)2-4R11, or (un)substituted heterocyclyl, aryl, or (cyclo)alkyl; R6 = NR7R8 or (un)substituted heterocyclyl, aryl, or (cyclo)alkyl; R7 and R8 = independently H, COR9, SO2R9, or (un)substituted aryl or (cyclo)alkyl; or NR7R8 = heterocyclyl; R9 = (un)substituted heterocyclyl, aryl, or (cyclo)alkyl; R11 = H or alkyl; R12 = H or (un)substituted heterocyclyl, aryl, or (cyclo)alkyl; or pharmaceutically acceptable salts thereof] were prepared For example, hydrogenation of 5-nitro-2-furonitrile was hydrogenated over 5% Pd/CaCO3, coupling of the amine with di-Et ethoxymethylenemalonate, cyclization, and addition of MeI gave Et 2-cyano-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate. Conversion of the nitrile to the aldehyde using Na hypophosphite and Raney-Ni, followed by reductive addition of morpholine provided the morpholinylmethyl derivative Amidation with 4-chlorobenzylamine afforded II. Representative compds. of the invention inhibited human cytomegalovirus (HCMV) polymerase in a scintillation proximity assay (no specific data). Thus, I are useful for the treatment of a herpesvirus infection, atherosclerosis, or restenosis (no data).

IC ICM C07D491-04
ICS A61K031-4355; A61P031-12

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST furopyridinecarboxamide prepn DNA polymerase inhibitor antiviral antiatherosclerotic; herpesvirus treatment furopyridinecarboxamide prepn

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT Infection
(herpes zoster; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT Drug delivery systems
(oral; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT Drug delivery systems
(parenterals; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT Antiviral agents
Atherosclerosis
Drug delivery systems
Human
Human herpesvirus 1
Human herpesvirus 2
Human herpesvirus 4
Human herpesvirus 5
Human herpesvirus 6
Human herpesvirus 7
Human herpesvirus 8
(preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT Artery, disease
(restenosis; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT Drug delivery systems
(topical; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT 562100-73-6P, N-(4-Chlorobenzyl)-2-[[[2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-05-7P, N-(4-Chlorobenzyl)-2-(chloromethyl)-7-ethyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-06-8P, N-(4-Chlorobenzyl)-2-(chloromethyl)-7-cyclopropyl-4-oxo-4,7-

dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-07-9P, N-(4-Chlorobenzyl)-2-(chloromethyl)-4-oxo-7-propyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-08-0P, N-(4-Chlorobenzyl)-2-(chloromethyl)-4-oxo-7-phenyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-09-1P, N-(4-Chlorobenzyl)-2-(chloromethyl)-4-oxo-7-(2-phenylethyl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-10-4P, N-(4-Chlorobenzyl)-2-(chloromethyl)-4-oxo-7-(pyridin-2-yl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-11-5P, N-(4-Chlorobenzyl)-2-(chloromethyl)-7-[2-(diethylamino)ethyl]-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide
RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antiviral agent; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT 562100-75-8P, (+)-N-(4-Chlorobenzyl)-2-[[[2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-76-9P, (-)-N-(4-Chlorobenzyl)-2-[[[2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiviral agent; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT 562101-12-6P, N-(4-Chlorobenzyl)-7-ethyl-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-13-7P, N-(4-Chlorobenzyl)-7-cyclopropyl-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-14-8P, N-(4-Chlorobenzyl)-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-4-oxo-7-propyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-15-9P, N-(4-Chlorobenzyl)-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-4-oxo-7-phenyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-16-0P, N-(4-Chlorobenzyl)-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-4-oxo-7-(2-phenylethyl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-17-1P, N-(4-Chlorobenzyl)-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-4-oxo-7-(pyridin-2-yl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-18-2P, N-(4-Chlorobenzyl)-7-[2-(diethylamino)ethyl]-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiviral agent; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT 562100-72-5P, N-(4-Chlorobenzyl)-2-(chloromethyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-98-5P, N-(4-Chlorobenzyl)-7-ethyl-2-(morpholin-4-ylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-99-6P, N-(4-Chlorobenzyl)-7-cyclopropyl-2-(morpholin-4-ylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-00-2P, N-(4-Chlorobenzyl)-7-propyl-2-(morpholin-4-ylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-01-3P, N-(4-Chlorobenzyl)-2-(morpholin-4-ylmethyl)-4-oxo-7-phenyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-02-4P, N-(4-Chlorobenzyl)-2-(morpholin-4-ylmethyl)-4-oxo-7-(2-phenylethyl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-03-5P, N-(4-Chlorobenzyl)-2-(morpholin-4-ylmethyl)-4-oxo-7-

(pyridin-2-yl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-04-6P, N-(4-Chlorobenzyl)-7-[2-(diethylamino)ethyl]-2-(morpholin-4-ylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-19-3P, N-(4-Chlorobenzyl)-2-[[(2-hydroxypropyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-67-1P, N-(4-Chlorobenzyl)-7-methyl-2-[(methylamino)methyl]-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-68-2P, N-(4-Chlorobenzyl)-2-[[(3-chloro-2-hydroxypropyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-74-0P, N-(4-Chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-75-1P, 2-Bromo-N-(4-chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-76-2P, N-(4-Chlorobenzyl)-2-(3-hydroxy-1-propynyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-78-4P, N-(4-Chlorobenzyl)-2-(4-hydroxy-1-butynyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-80-8P, N-(4-Chlorobenzyl)-2-(5-hydroxy-1-pentynyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-82-0P, N-(4-Chlorobenzyl)-2-(3-hydroxy-3-phenyl-1-propynyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-84-2P, N-(4-Chlorobenzyl)-2-(4-hydroxy-4-phenyl-1-butynyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(antiviral agent; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT 562100-71-4P, N-(4-Chlorobenzyl)-7-methyl-2-(4-morpholinylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-79-2P, N-(4-Fluorobenzyl)-2-[[[(2R)-2-(2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-80-5P, 2-[[[(2R)-2-(2-Furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-N-(4-methylbenzyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-81-6P, 2-[[[(2R)-2-(2-Furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-N-(3,4-difluorobenzyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-82-7P, 2-[[[(2R)-2-(2-Furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-N-(3,4-dichlorobenzyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-83-8P, 2-[[[(2R)-2-(2-Furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-N-(4-bromobenzyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562100-84-9P, 2-[[[(2R)-2-(2-Furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-N-(4-trifluoromethylbenzyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-20-6P, N-(4-Chlorobenzyl)-2-[[(2-hydroxypropyl)(methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-21-7P, N-(4-Chlorobenzyl)-2-[((3R)-3-hydroxypyrrolidin-1-yl)methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-22-8P, N-(4-Chlorobenzyl)-2-[[(2-hydroxy-2-phenylethyl)(methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-23-9P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(4-hydroxyphenyl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-45-5P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(3-methoxyphenyl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-46-6P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(pyridin-2-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-47-7P, N-(4-Chlorobenzyl)-2-[[[(2R)-2-hydroxy-2-(pyridin-2-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-48-8P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(pyridin-3-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-

b]pyridine-5-carboxamide 562101-49-9P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(5-methyl-2-furyl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-50-2P, N-(4-Chlorobenzyl)-2-[[[2-(3-furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-51-3P, 2-[[[2-(Benzofuran-2-yl)-2-hydroxyethyl](methyl)amino]methyl]-N-(4-chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-52-4P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(thien-2-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-53-5P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(quinolin-2-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-54-6P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(1-methyl-1H-pyrrol-2-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-55-7P, N-(4-Chlorobenzyl)-2-[[[2-(5-cyanothien-2-yl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-56-8P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(1,3-thiazol-2-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-57-9P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(5-phenyl-2-furyl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-58-0P, N-(4-Chlorobenzyl)-2-[[[2-(4,5-dimethyl-2-furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-59-1P 562101-60-4P 562101-62-6P, N-(4-Chlorobenzyl)-2-[[(3-hydroxy-2-phenylpropyl)(methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-66-0P 562101-69-3P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-3-[(2-methoxyphenyl)thio]propyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-71-7P, 2-[[[3-[(5-Amino-1,3,4-thiadiazol-2-yl)thio]-2-hydroxypropyl](methyl)amino]methyl]-N-(4-chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-72-8P, 2-[[[3-[(3-Amino-1H-1,2,4-triazol-5-yl)thio]-2-hydroxypropyl](methyl)amino]methyl]-N-(4-chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-73-9P, 2-[[[3-[(4-Aminopyrimidin-2-yl)thio]-2-hydroxypropyl](methyl)amino]methyl]-N-(4-chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-77-3P, N-(4-Chlorobenzyl)-2-(3-hydroxypropyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-79-5P, N-(4-Chlorobenzyl)-2-(4-hydroxybutyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-81-9P, N-(4-Chlorobenzyl)-2-(5-hydroxypentyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-83-1P, N-(4-Chlorobenzyl)-2-(3-hydroxy-3-phenylpropyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-85-3P, N-(4-Chlorobenzyl)-2-(4-hydroxy-4-phenylbutyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-86-4P, N-(4-Chlorobenzyl)-2-(ethoxymethyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-87-5P, N-(4-Chlorobenzyl)-2-(hydroxymethyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-88-6P, N-(4-Chlorobenzyl)-2-[[((2S)-2-hydroxy-2-phenylethyl)oxy]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-89-7P, N-[(4-Chlorophenyl)methyl]-5-[[[(4-chlorophenyl)methyl]amino]carbonyl]-4-hydroxyfuro[2,3-b]pyridine-2-carboxamide 562101-91-1P, N-(4-Chlorobenzyl)-2-[[[2-(4-fluorophenyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-92-2P, N-(4-Chlorobenzyl)-2-[[[2-(4-chlorophenyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-93-3P,

N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(pyridin-4-yl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-94-4P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-2-(2,4,6-trifluorophenyl)ethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-95-5P 562101-96-6P, N-(4-Chlorobenzyl)-2-[[(2R)-2-[(R)-hydroxy(pyridin-2-yl)methyl]pyrrolidin-1-yl]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-97-7P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-3-[(3-methoxyphenyl)thio]propyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-98-8P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-3-[(4-methoxyphenyl)thio]propyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562101-99-9P, 2-[[3-[[[5-[[(4-Chlorobenzyl)amino]carbonyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridin-2-yl]methyl](methyl)amino]-2-hydroxypropyl]thio]benzoic acid 562102-00-5P, 2-[[3-[[[5-[[(4-Chlorobenzyl)amino]carbonyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridin-2-yl]methyl](methyl)amino]-2-hydroxypropyl]thio]nicotinic acid 562102-01-6P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-3-[(4-oxo-3,4-dihydroquinazolin-2-yl)thio]propyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-02-7P, 2-[[[3-[(6-Amino-1,3-benzothiazol-2-yl)thio]-2-hydroxypropyl](methyl)amino]methyl]-N-(4-chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-03-8P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-3-[(9H-purin-6-yl)thio]propyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-04-9P, 2-[[[3-(Benzylthio)-2-hydroxypropyl](methyl)amino]methyl]-N-(4-chlorobenzyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-05-0P, N-(4-Chlorobenzyl)-2-[[[3-[(4-chlorobenzyl)thio]-2-hydroxypropyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-06-1P, N-(4-Chlorobenzyl)-2-[[[2-hydroxy-3-[(4-methoxybenzyl)thio]propyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-07-2P, N-(4-Chlorobenzyl)-2-[4-(2-furyl)-4-hydroxy-1-butynyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-08-3P, N-(4-Chlorobenzyl)-2-[4-(2-furyl)-4-hydroxybutyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-09-4P, N-(4-Chlorobenzyl)-2-[4-hydroxy-4-(pyridin-3-yl)-1-butynyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-10-7P, N-(4-Chlorobenzyl)-2-[4-hydroxy-4-(pyridin-3-yl)butyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-11-8P, N-(4-Chlorobenzyl)-2-[4-hydroxy-4-(pyridin-2-yl)-1-butynyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide 562102-12-9P, N-(4-Chlorobenzyl)-2-[4-hydroxy-4-(pyridin-2-yl)butyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiviral agent; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT 451-45-6P, 1-(4-Fluorophenyl)-2-(methylamino)ethanol 1634-53-3P, 2-Bromo-1-(5-methyl-2-furyl)ethanone 1743-32-4P, 1-(2-Furyl)-3-butyn-1-ol 2745-40-6P, 1-(2-Furyl)-2-(methylamino)ethanol 6314-52-9P, 2-Bromo-1-(4-chlorophenyl)ethanol 19313-32-7P, 2-(Methylamino)-1-(thien-2-yl)ethanol 31491-45-9P, 2-Chloro-3-furoic acid 34071-56-2P, Ethyl 7-Ethyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 36695-59-7P, 2-(Methylamino)-1-(pyridin-4-yl)ethanol 40587-06-2P, 1-(4-Chlorophenyl)-2-(methylamino)ethanol 42511-14-8P, 3-(Methylamino)-2-phenylpropan-1-ol 53617-32-6P, 2-Bromo-1-(4-fluorophenyl)ethanol 55967-97-0P 57591-47-6P,

3-Amino-2-phenylpropan-1-ol 58777-49-4P, 2-Furoyl bromide 89242-75-1P, 1-(Pyridin-3-yl)-3-butyn-1-ol 92188-49-3P, 1-(3-Methoxyphenyl)-2-(methylamino)ethanol 94829-51-3P 113864-94-1P, 2-[(Hydroxy)(phenyl)methyl]pyrrolidine 118838-55-4P 118838-57-6P 126353-32-0P, 2-Bromo-1-(pyrazin-2-yl)ethanone Hydrobromide 158397-53-6P 496879-84-6P, 5-(Bromoacetyl)thiophene-2-carbonitrile 517907-46-9P, 1-(Pyridin-2-yl)-3-butyn-1-ol 556025-48-0P, 1-(1-Benzofuran-2-yl)-2-(methylamino)ethanol 556025-49-1P, 1-(3-Furyl)-2-(methylamino)ethanol 556025-50-4P, 2-(Methylamino)-1-(5-methyl-2-furyl)ethanol 556025-54-8P, (1R)-1-(2-Furyl)-2-(methylamino)ethanol 556025-58-2P, 2-(Methylamino)-1-(quinolin-2-yl)ethanol 556025-60-6P, 5-[1-Hydroxy-2-(methylamino)ethyl]thiophene-2-carbonitrile 556025-61-7P, (1R)-2-(Methylamino)-1-(pyrazin-2-yl)ethanol 556025-69-5P, 5-(2-Bromo-1-hydroxyethyl)thiophene-2-carbonitrile 556025-79-7P, (5R)-5-(2-Furyl)-3-methyl-1,3-oxazolidin-2-one 556025-92-4P, 2-Chloro-1-(1,3-thiazol-2-yl)ethanone 562100-62-3P, 5-Amino-2-furonitrile 562100-63-4P, Diethyl 2-[[(5-Cyano-2-furyl)amino]methylene]malonate 562100-64-5P, Ethyl 2-Cyano-4-hydroxyfuro[2,3-b]pyridine-5-carboxylate 562100-65-6P, Ethyl 2-Cyano-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-66-7P, Ethyl 2-Formyl-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-67-8P, Ethyl 7-Methyl-4-oxo-2-(4-morpholinylmethyl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-68-9P, Ethyl 3-(2-Chloro-3-furyl)-3-oxopropanoate 562100-69-0P, Ethyl 7-Methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-74-7P 562100-77-0P, Ethyl 2-(Chloromethyl)-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-78-1P, Ethyl 2-[[[(2R)-2-(2-Furyl)-2-hydroxyethyl](methyl)amino]methyl]-7-methyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-85-0P, Ethyl 7-Cyclopropyl-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-86-1P, Ethyl 4-Oxo-7-propyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-87-2P, Ethyl 4-Oxo-7-phenyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-88-3P, Ethyl 4-Oxo-7-(2-phenylethyl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-89-4P, Ethyl 4-Oxo-7-(pyridin-2-yl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-90-7P, Ethyl 7-[2-(Diethylamino)ethyl]-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-91-8P, Ethyl 7-Ethyl-2-(morpholin-4-ylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-92-9P, Ethyl 7-Cyclopropyl-2-(morpholin-4-ylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-93-0P, Ethyl 2-(Morpholin-4-ylmethyl)-4-oxo-7-propyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-94-1P, Ethyl 2-(Morpholin-4-ylmethyl)-4-oxo-7-phenyl-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-95-2P, Ethyl 2-(Morpholin-4-ylmethyl)-4-oxo-7-(2-phenylethyl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-96-3P, Ethyl 2-(Morpholin-4-ylmethyl)-4-oxo-7-(pyridin-2-yl)-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562100-97-4P, Ethyl 7-[2-(Diethylamino)ethyl]-2-(morpholin-4-ylmethyl)-4-oxo-4,7-dihydrofuro[2,3-b]pyridine-5-carboxylate 562101-24-0P, 2-(Methylamino)-1-(pyridin-2-yl)ethanol 562101-25-1P, (1R)-2-(Methylamino)-1-(pyridin-2-yl)ethanol (2S)-2-(6-Methoxy-2-naphthyl)propanoic acid salt 562101-26-2P, (R)-2-(Methylamino)-1-(pyridin-2-yl)ethanol dihydrochloride 562101-27-3P, 2-(Methylamino)-1-(pyridin-3-yl)ethanol hydrobromide 562101-28-4P, 2-(Methylamino)-1-(2,4,6-trifluorophenyl)ethanol 562101-29-5P, 2-(Methylamino)-1-(1-methyl-1H-pyrrol-2-yl)ethanol 562101-31-9P, 2-(Methylamino)-1-(1,3-thiazol-2-yl)ethanol 562101-32-0P, 3-Methyl-5-(5-phenyl-2-furyl)-1,3-oxazolidin-2-one 562101-33-1P, 2-(Methylamino)-1-(5-phenyl-2-furyl)ethanol 562101-34-2P, 5-(4,5-Dimethyl-2-furyl)-3-methyl-1,3-oxazolidin-2-

one 562101-35-3P, 1-(4,5-Dimethyl-2-furyl)-2-(methylamino)ethanol 562101-36-4P, tert-Butyl N-[2-(pyrazin-2-yl)-2-oxoethyl]-N-methylcarbamate 562101-37-5P, tert-Butyl [(2R)-2-hydroxy-2-(pyrazin-2-yl)ethyl](methyl)carbamate 562101-38-6P, Sodium pyrimidine-2-carboxylate 562101-39-7P, N-Methoxy-N-methylpyrimidine-2-carboxamide 562101-40-0P, 4-(Pyrimidin-2-ylcarbonyl)morpholine 562101-41-1P 562101-42-2P, tert-Butyl N-[2-(pyrimidin-2-yl)-2-oxoethyl]-N-methylcarbamate 562101-43-3P, tert-Butyl [(2R)-2-hydroxy-2-(pyrimidin-2-yl)ethyl](methyl)carbamate 562101-44-4P, (1R)-2-(Methylamino)-1-(pyrimidin-2-yl)ethanol Dihydrochloride 562101-61-5P, Ethyl (3-Hydroxy-2-phenylpropyl)carbamate 562101-63-7P, N-Boc-2-[(hydroxy)(phenyl)methyl]pyrrolidine 562101-64-8P, (2-Furyl)(pyrrolidin-2-yl)methanol 562101-65-9P, (2-Furyl)(N-Boc-pyrrolidin-2-yl)methanol 562102-13-0P, (1R)-2-(Methylamino)-1-(pyrimidin-2-yl)ethanol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

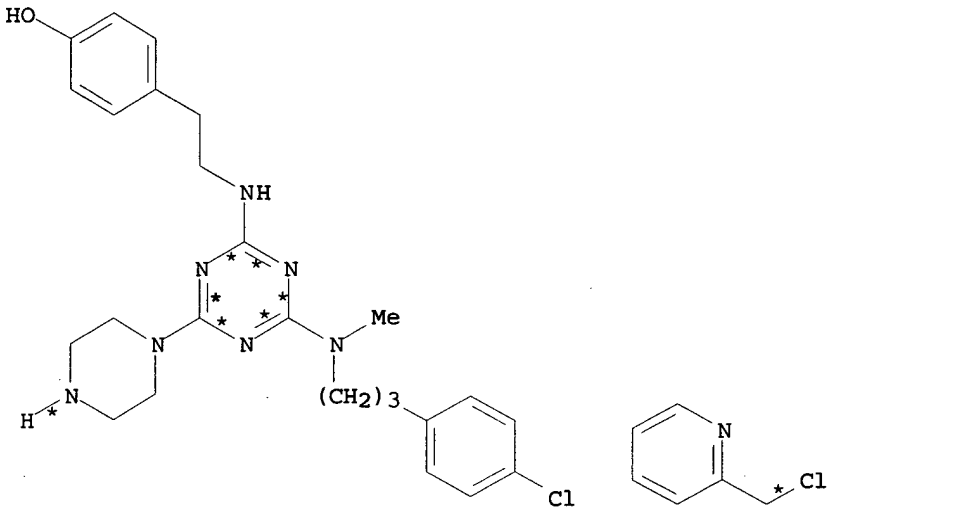
IT 59-82-5, 5-Nitro-2-furonitrile 62-53-3, Aniline, reactions 64-04-0, Phenethylamine 78-96-6, 1-Amino-2-propanol 87-13-8, Diethyl ethoxymethylenemalonate 98-01-1, 2-Furaldehyde, reactions 98-03-3, Thiophene-2-carboxaldehyde 100-36-7, N,N-Diethylethylenediamine 100-52-7, Benzaldehyde, reactions 100-69-6, 2-Vinylpyridine 102-49-8, 3,4-Dichlorobenzylamine 104-84-7, 4-Methylbenzylamine 104-86-9, 4-Chlorobenzylamine 106-96-7, Propargyl bromide 107-10-8, Propylamine, reactions 107-19-7, Propargyl alcohol 108-98-5, Thiophenol, reactions 110-91-8, Morpholine, reactions 140-75-0, 4-Fluorobenzylamine 333-49-3, 4-Amino-2-mercaptopyrimidine 403-29-2, 2-Bromo-4'-fluoroacetophenone 488-93-7, 3-Furoic acid 498-60-2, 3-Furaldehyde 500-22-1, 3-Pyridinecarboxaldehyde 504-29-0, 2-Aminopyridine 536-38-9, 2-Bromo-4'-chloroacetophenone 541-41-3, Ethyl chloroformate 765-30-0, Cyclopropylamine 927-74-2, 3-Butyn-1-ol 1121-60-4, 2-Pyridinecarboxaldehyde 1192-62-7, 2-Acetylfuran 1193-79-9, 2-Acetyl-5-methylfuran 1743-36-8, 1-Phenyl-3-butyn-1-ol 2349-67-9, 5-Amino-1,3,4-thiadiazole-2-thiol 2799-21-5, (R)-3-Hydroxypyrrolidine 3300-51-4, 4-Trifluoromethylbenzylamine 4187-87-5, 1-Phenyl-2-propyn-1-ol 4265-16-1, Benzofuran-2-carboxaldehyde 4553-07-5 5349-17-7, 4-Bromoacetylpyridine hydrobromide 5390-04-5, 4-Pentyn-1-ol 5470-96-2, 2-Quinolinecarboxaldehyde 6148-64-7, Potassium ethyl malonate 6589-55-5, α-[(Methylamino)methyl]benzyl alcohol 7217-59-6, 2-Methoxythiophenol 7541-17-5, tert-Butyl dimethylcarbamate 13803-39-9, 5-Phenyl-2-furancarboxaldehyde 14080-23-0, 2-Cyanopyrimidine 16589-24-5 16691-43-3, 3-Amino-5-mercapto-1,2,4-triazole 17570-98-8, 2-Bromoacetylpyridine hydrobromide 17694-68-7, 3-Bromoacetylpyridine hydrobromide 22047-25-2, 2-Acetylpyrazine 22204-53-1, (S)-Naproxen 25779-13-9, (S)-1-Phenyl-1,2-ethanediol 26177-44-6, 4-Bromobenzylamine hydrochloride 32017-77-9, (3-Methoxyphenyl)oxirane 52853-19-7, 4-Methylenemorpholin-4-ium chloride 58551-83-0, 2,4,6-Trifluorobenzaldehyde 72235-53-1, 3,4-Difluorobenzylamine 79265-30-8, 2-(Trimethylsilyl)thiazole 86953-79-9 88653-55-8, 2-Acetyl-5-cyanothiophene 90197-12-9, 2-(Methylamino)-1-(pyridin-3-yl)ethanol 139683-93-5, (R)-2-Amino-1-(2-furyl)ethanol 562101-30-8, 2-Chloro-1-(1-methyl-1H-pyrrol-2-yl)ethanol 562101-90-0, Furo[2,3-b]pyridine-2-carboxylic acid methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

IT 9012-90-2, DNA polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(viral, inhibitors; preparation of furo[2,3-b]pyridinecarboxamide DNA polymerase inhibitors as antiviral agents)

L40 ANSWER 11 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

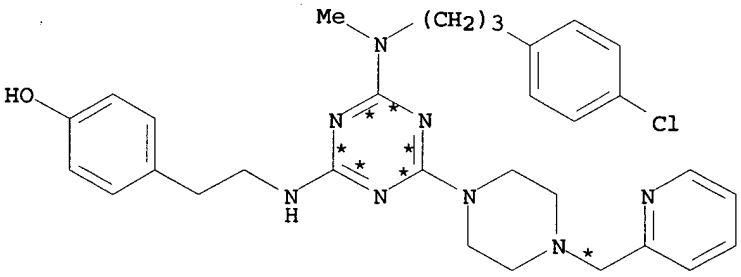
RX(11) OF 37 ...**U** + AE ===> **AF**



U

AE

(11)



AF
YIELD 45%

RX(11) RCT **U 459873-38-2**, AE 4377-33-7

STAGE(1)
RGT AG 7087-68-5 EtN(Pr-i)2
SOL 75-09-2 CH2Cl2
CON 1 hour, room temperature

STAGE(2)
SOL 75-05-8 MeCN
CON 5 hours, 80 deg C

PRO AF **459872-91-4**
ACCESSION NUMBER: 138:32798 CASREACT
TITLE: A new series of estrogen receptor modulators

that display selectivity for estrogen receptor β

AUTHOR(S): Henke, Brad R.; Consler, Thomas G.; Go, Ning; Hale, Ron L.; Hohman, Dana R.; Jones, Stacey A.; Lu, Amy T.; Moore, Linda B.; Moore, John T.; Orband-Miller, Lisa A.; Robinett, R. Graham; Shearin, Jean; Spearing, Paul K.; Stewart, Eugene L.; Turnbull, Philip S.; Weaver, Susan L.; Williams, Shawn P.; Wisely, G. Bruce; Lambert, Millard H.

CORPORATE SOURCE: GlaxoSmithKline Research and Development, Research Triangle Park, NC, 27709, USA

SOURCE: Journal of Medicinal Chemistry (2002), 45(25), 5492-5505
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 1,3,5-triazine-based estrogen receptor (ER) modulators that are modestly selective for the ERβ subtype are reported. The triazine-derived ER Compound, which displayed modest potency and selectivity for ERβ vs. ERα, was identified via high-throughput screening utilizing an ERβ SPA-based binding assay. Subsequent analog preparation resulted in the identification of compds. such as that display 25- to 30-fold selectivity for ERβ with potencies in the 10-30 nM range. These compds. profile as full antagonists at ERβ and weak partial agonists at ERα in a cell-based reporter gene assay. In addition, the x-ray crystal structure of one of the compds. complexed with the ligand binding domain of ERβ has been solved and was utilized in the design of more conformationally restrained analogs in an attempt to increase selectivity for the ERβ subtype.

CC 1-3 (Pharmacology)

ST triazine deriv prepn structure activity estrogen receptor modulator

IT Conformers
Crystal structure
Drug design
High throughput screening
Molecular modeling
Molecular structure
Structure-activity relationship
(structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α; structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β; structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

IT 459873-38-2P
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

IT 459872-91-4P 459872-93-6P 459872-95-8P 459873-05-3P
459873-07-5P 459873-20-2P 459873-34-8P 459873-40-6P
478625-38-6P 478625-40-0P 478625-42-2P 478625-44-4P
478625-46-6P 478625-48-8P 478625-50-2P 478625-52-4P

478625-54-6P 478625-56-8P 478625-59-1P 478625-61-5P
478625-62-6P 478625-63-7P 478625-64-8P 478625-67-1P
478625-69-3P 478625-71-7P 478625-74-0P 478625-76-2P
478625-78-4P 478625-80-8P 478625-83-1P 478625-85-3P
478625-87-5P 478625-89-7P 478625-92-2P 478625-95-5P
478625-97-7P 478625-99-9P 478626-00-5P 478626-02-7P
478626-04-9P 478626-11-8P 478626-15-2P 478626-17-4P
478626-18-5P 478626-20-9P 478626-22-1P 478626-24-3P
478626-26-5P 478626-28-7P 478626-31-2P 478626-33-4P
478626-35-6P 478626-37-8P 478626-39-0P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

IT 51-67-2 100-46-9, Benzylamine, reactions 108-77-0 109-01-3, N-Methylpiperazine 603-35-0, reactions 696-60-6 939-90-2
1822-51-1, 4-Chloromethylpyridine hydrochloride 2019-34-3
2033-76-3 2472-22-2 4361-44-8, Cyclohexanepropanamine
4377-33-7, 2-Chloromethylpyridine 6959-48-4,
3-Chloromethylpyridine hydrochloride 13484-40-7 18655-48-6
18655-50-0 21043-40-3, 1-Cyclopentyl piperazine 23363-75-9,
4-Cyanocinnamoyl chloride 23530-40-7 56553-60-7 57260-71-6
77470-53-2 78498-59-6, 1,3-Benzodioxole-5-propanamine
101488-60-2 101488-65-7 147498-88-2 175219-67-7
377083-92-6 459872-75-4 478626-41-4 478626-43-6
478626-45-8 478626-50-5 478626-52-7 478626-54-9
478626-80-1 478627-02-0 478627-04-2 478627-07-5
478627-09-7 478627-11-1 478627-13-3 478627-15-5
478627-17-7 478627-19-9 478627-21-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

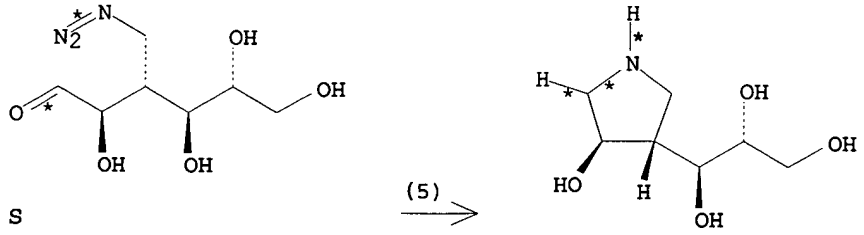
IT 175219-66-6P 271592-49-5P 459872-34-5P 459872-53-8P
459872-63-0P 478626-83-4P 478626-95-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

IT 15639-82-4P 33543-11-2P 65686-13-7P 70312-01-5P
90944-90-4P 103273-66-1P 459872-39-0P 459872-41-4P
459872-43-6P 459872-45-8P 459872-47-0P 459872-55-0P
459872-56-1P 459872-61-8P 459872-65-2P 459872-77-6P
459872-81-2P 459873-24-6P 478626-68-5P 478626-71-0P
478626-73-2P 478626-92-5P 478626-98-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(structure-activity relationship of triazine-based estrogen receptor modulators that display selectivity for estrogen receptor β)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 12 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(5) OF 90 ...S ===> U...



S (5) U

YIELD 80%

RX(5) RCT S 395076-04-7
RGT V 1333-74-0 H2
PRO U 362600-27-9
CAT **7440-05-3** Pd
SOL 7732-18-5 Water
NTE high pressure

ACCESSION NUMBER: 136:151380 CASREACT
TITLE: Synthesis of 1'-aza-C-nucleosides from (3R,4R)-4-(hydroxymethyl)pyrrolidin-3-ol
AUTHOR(S): Filichev, Vyacheslav V.; Pedersen, Erik B.
CORPORATE SOURCE: Department of Chemistry, University of Southern Denmark, Odense University, Odense, DK-5230, Den.
SOURCE: Tetrahedron (2001), 57(44), 9163-9168
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pyrimidine 1'-aza-C-nucleosides are synthesized by the fusion of 5-bromouracil, 5-bromocytosine and 5-bromoisocytosine with (3R,4R)-4-(hydroxymethyl)pyrrolidin-3-ol in 40-41% yield. A homolog of 1'-aza-Ψ-uridine is obtained in a Mannich reaction in 65% yield by treatment of the azasugar, paraformaldehyde and uracil. N-Alkylation of (3R,4R)-4-(hydroxymethyl)pyrrolidin-3-ol with 6-chloromethyluracil gives the 6-regioisomeric homolog. (3R,4R)-4-(Hydroxymethyl)pyrrolidin-3-ol is synthesized in 25% overall yield from diacetone-D-glucose via 3-C-(azidomethyl)-3-deoxy-D-allose which is subjected to an intramol. reductive amino alkylation reaction to give (3R,4S)-4-[(1S,2R)-1,2,3-trihydroxypropyl]pyrrolidin-3-ol followed by Fmoc protection, oxidative cleavage of the triol group with further reduction of the obtained aldehyde and subsequent deprotection of the nitrogen atom.

CC 33-9 (Carbohydrates)
Section cross-reference(s): 27, 28

ST bromopyrimidine condensation hydroxymethylpyrrolidinol; hydroxymethyl pyrrolidinol prepn intramol reductive amino alkylation; pyrimidine aza C nucleoside prepn

IT C-nucleosides
RL: SPN (Synthetic preparation); PREP (Preparation)
(1'-aza-; synthesis of 1'-aza-C-nucleosides via fusion of bromopyrimidines and (3R,4R)-4-(hydroxymethyl)pyrrolidinol)

IT Alkylation
(reductive, intramol.; synthesis of 1'-aza-C-nucleosides via fusion of bromopyrimidines and (3R,4R)-4-(hydroxymethyl)pyrrolidinol)

IT 51-20-7, 5-Bromouracil 66-22-8, Uracil, reactions 582-52-5 2240-25-7, 5-Bromocytosine 18592-13-7, 6-Chloromethyluracil 61937-71-1 162284-62-0
RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of 1'-aza-C-nucleosides via fusion of bromopyrimidines and (3R,4R)-4-(hydroxymethyl)pyrrolidinol)

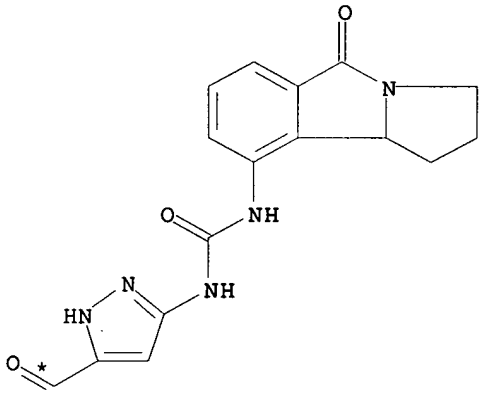
IT 21665-16-7P 180403-62-7P 214134-59-5P 267421-93-2P 362600-15-5P 362600-27-9P 395076-04-7P 395076-07-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 1'-aza-C-nucleosides via fusion of bromopyrimidines and (3R,4R)-4-(hydroxymethyl)pyrrolidinol)

IT 395076-11-6P 395076-13-8P 395076-15-0P 395076-17-2P 395076-20-7P 395076-22-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 1'-aza-C-nucleosides via fusion of bromopyrimidines and (3R,4R)-4-(hydroxymethyl)pyrrolidinol)

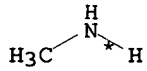
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 13 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(8) OF 101 ...AD + AF ===> AG

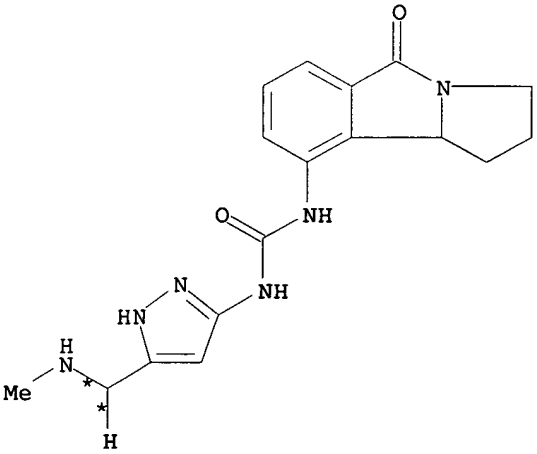


AD



AF

(8)



AG

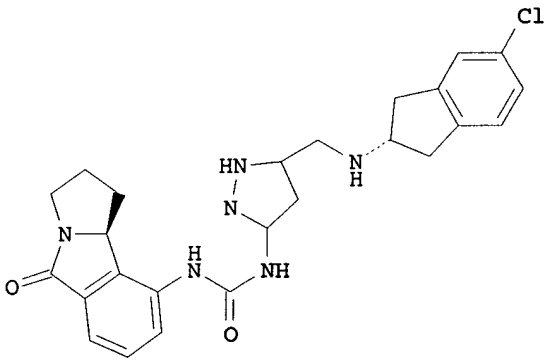
RX(8) RCT AD 322693-26-5, AF 74-89-5

STAGE(1)
SOL 67-56-1 MeOH

STAGE(2)
RGT AH **16940-66-2** NaBH4

PRO AG 322689-80-5

ACCESSION NUMBER: 136:146987 CASREACT
TITLE: A Novel Approach for the Development of Selective Cdk4 Inhibitors: Library Design Based on Locations of Cdk4 Specific Amino Acid Residues
AUTHOR(S): Honma, Teruki; Yoshizumi, Takashi; Hashimoto, Noriaki; Hayashi, Kyoko; Kawanishi, Nobuhiko; Fukasawa, Kazuhiro; Takaki, Tohru; Ikeura, Chinatsu; Ikuta, Mari; Suzuki-Takahashi, Ikuko; Hayama, Takashi; Nishimura, Susumu; Morishima, Hajime
CORPORATE SOURCE: Banyu Tsukuba Research Institute in collaboration with Merck Research Laboratories, Tsukuba, Ibaraki, 300-2611, Japan
SOURCE: Journal of Medicinal Chemistry (2001), 44(26), 4628-4640
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Identification of a selective inhibitor for a particular protein kinase without inhibition of other kinases is critical for use as a biol. tool or drug. However, this is very difficult because there are hundreds of homologous kinases and their kinase domains including the ATP binding pocket have a common folding pattern. To address this issue, the authors applied the following structure-based approach for designing selective Cdk4 inhibitors: (1) identification of specifically altered amino acid residues around the ATP binding pocket in Cdk4 by comparison of 390 representative kinases, (2) prediction of appropriate positions to introduce substituents in lead compds. based on the locations of the altered amino acid residues and the binding modes of lead compds., and (3) library design to interact with the altered amino

acid residues supported by de novo design programs. Accordingly, Asp99, Thr102, and Gln98 of Cdk4, which are located in the p16 binding region, were selected as first target residues for specific interactions with Cdk4. Subsequently, the 5-position of the pyrazole ring in the pyrazol-3-ylurea class of lead compound was predicted to be a suitable position to introduce substituents. The authors then designed a chemical library of pyrazol-3-ylurea substituted with alkylaminomethyl groups based on the output structures of de novo design programs. Thus the authors identified a highly selective and potent Cdk4 inhibitor (I), substituted with a 5-chloroindan-2-ylaminomethyl group. Compound I showed higher selectivity on Cdk4 over those on not only Cdk1/2 (780-fold/190-fold) but also many other kinases (>430-fold) that have been tested thus far. The structural basis for Cdk4 selective inhibition by I was analyzed by combining mol. modeling and the x-ray anal. of the Cdk4 mimic Cdk2-inhibitor complex. The results suggest that the hydrogen bond with the carboxyl group of Asp99 and hydrophobic van der Waals contact with the side chains of Thr102 and Gln98 are important. Compound I was found to cause cell cycle arrest of the Rb(+) cancer cell line in the G1 phase, indicating that it is a good biol. tool.

CC 7-3 (Enzymes)
Section cross-reference(s): 1, 28

ST Cdk4 kinase inhibitor design pyrazolylurea structure

IT Structure-activity relationship
(Cdk4 kinase-inhibiting; novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT Antitumor agents
Drug design
Enzyme functional sites
Hydrogen bond
Molecular association
Molecular modeling
Protein sequences
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p16INK4A, Cdk4 kinase binding by; novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT 144378-32-5, Cyclin B-Cdk1 kinase 146279-88-1, Cyclin A-Cdk2 kinase 153190-74-0, Cyclin D2-Cdk4 kinase 166433-52-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT 391937-50-1
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT 393590-58-4P 393590-60-8P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT 322689-01-0P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT 322689-07-6P 322689-72-5P 322689-74-7P 322689-75-8P 322689-76-9P 322689-78-1P 322689-79-2P 322689-80-5P 322689-82-7P 393590-69-7P 393590-70-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT 75-05-8, Acetonitrile, reactions 122-04-3, p-Nitrobenzoyl chloride 955-40-8, N-Benzyl-proline ethyl ester 2975-41-9, 2-Aminoindan 21377-09-3 24424-99-5, Di-tert-butyl dicarbonate 32122-09-1, Ethyl benzyl oxyacetate 322692-77-3 391937-46-5 391937-47-6 393590-59-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

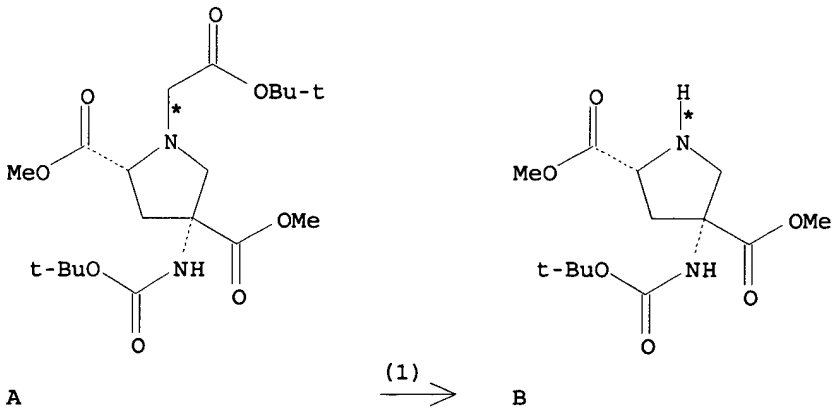
IT 73536-83-1P 322688-41-5P 322692-22-8P 322693-26-5P 393590-61-9P 393590-62-0P 393590-63-1P 393590-64-2P 393590-65-3P 393590-66-4P 393590-67-5P 393590-68-6P 393590-71-1P 393590-73-3P 393590-74-4P 393590-75-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

IT 393590-72-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(novel approach for development of selective Cdk4 inhibitors and library design of pyrazolylureas based on locations of Cdk4 specific amino acid residues in relation to antitumor activity)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 14 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(1) OF 57 A ===> B...



A B

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PRO B 238753-27-0
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SOL 67-56-1 MeOH

ACCESSION NUMBER: 135:338726 CASREACT
TITLE: Synthesis of N1-substituted analogues of (2R,4R)-4-amino-pyrrolidine-2,4-dicarboxylic acid as agonists, partial agonists, and antagonists of group II metabotropic glutamate receptors
AUTHOR(S): Mukhopadhyaya, J. K.; Kozikowski, A. P.; Grajkowska, E.; Pshenichkin, S.; Wroblewski, J. T.
CORPORATE SOURCE: Department of Neurology, Drug Discovery Program, Georgetown University Medical Center, Washington, DC, 20007, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(14), 1919-1924
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chemical synthesis of a series of N1-substituted derivs. of (2R,4R)-4-aminopyrrolidine-2,4-dicarboxylic acid [(2R,4R)-APDC] as constrained analogs of γ-substituted glutamic acids is described. Appropriate substitution of the N1-position results in agonist, partial agonist, or antagonist activity at mGluR2, mGluR3, and/or mGluR6.

CC 1-3 (Pharmacology)
Section cross-reference(s): 27

ST aminopyrrolidine dicarboxylic acid prepn metabotropic glutamate receptor ligand

IT Glutamate agonists
Glutamate antagonists
(mGluR2, mGluR3, and mGluR6; synthesis of N1-substituted analogs of (2R,4R)-4-amino-pyrrolidine-2,4-dicarboxylic acid as agonists, partial agonists, and antagonists of group II metabotropic glutamate receptors)

IT Structure-activity relationship
(synthesis of N1-substituted analogs of (2R,4R)-4-amino-pyrrolidine-2,4-dicarboxylic acid as agonists, partial agonists, and antagonists of group II metabotropic glutamate receptors)

IT 371979-01-0P 371979-02-1P 371979-03-2P 371979-04-3P
371979-05-4P 371979-06-5P 371979-07-6P 371979-08-7P
371979-09-8P 371979-10-1P 371979-11-2P 371979-12-3P
371979-13-4P 371979-14-5P 371979-15-6P 371979-16-7P
371979-17-8P 371979-18-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of N1-substituted analogs of (2R,4R)-4-amino-pyrrolidine-2,4-dicarboxylic acid as agonists, partial agonists, and antagonists of group II metabotropic glutamate receptors)

IT 169209-63-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of N1-substituted analogs of (2R,4R)-4-amino-pyrrolidine-2,4-dicarboxylic acid as agonists, partial agonists, and antagonists of group II metabotropic glutamate receptors)

IT 51-35-4

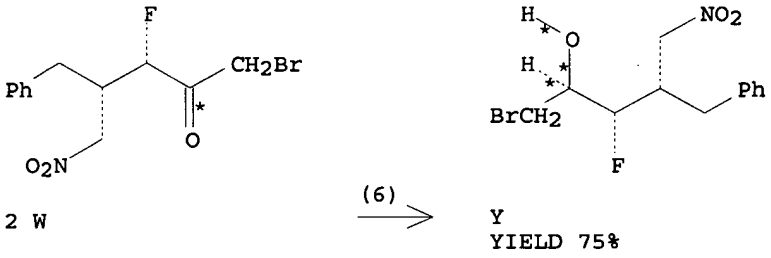
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of N1-substituted analogs of (2R,4R)-4-amino-pyrrolidine-2,4-dicarboxylic acid as agonists, partial agonists, and antagonists of group II metabotropic glutamate receptors)

IT 238753-27-0P 371978-97-1P 371978-98-2P 371978-99-3P
371979-00-9P 371979-19-0P 371979-20-3P 371979-21-4P
371979-22-5P 371979-23-6P 371979-24-7P 371979-25-8P
371979-26-9P 371979-27-0P 371979-28-1P 371979-29-2P
371979-30-5P 371979-31-6P 371979-32-7P 371979-33-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of N1-substituted analogs of (2R,4R)-4-amino-pyrrolidine-2,4-dicarboxylic acid as agonists, partial agonists, and antagonists of group II metabotropic glutamate receptors)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

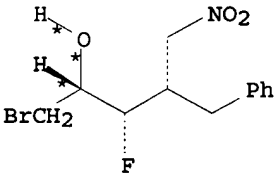
L40 ANSWER 15 OF 15 CASREACT COPYRIGHT 2006 ACS on STN

RX(6) OF 567 ...2 W ===> Y + Z...



2 W

Y
YIELD 75%



Z
YIELD 15%

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PRO Y 360558-20-9, Z 360558-21-0
SOL 64-17-5 EtOH
NTE stereoselective

ACCESSION NUMBER: 135:242482 CASREACT
TITLE: Asymmetric Synthesis of Chiral Organofluorine Compounds: Use of Nonracemic Fluoroiodoacetic Acid as a Practical Electrophile and Its Application to the Synthesis of Monofluoro Hydroxyethylene Dipeptide Isosteres within a Novel Series of HIV Protease Inhibitors
AUTHOR(S): Myers, Andrew G.; Barbay, Joseph K.; Zhong, Boyu

CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (2001), 123(30), 7207-7219
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Two stereoselective routes to a series of diastereomeric inhibitors of HIV protease, monofluorinated analogs of the Merck HIV protease inhibitor indinavir, are described. The two routes feature stereoselective construction of the fluorinated core subunits by asym. alkylation reactions. The first-generation syntheses were based on the conjugate addition of the lithium enolate derived from pseudoephedrine α-fluoroacetamide to trans-nitroalkene Ph-CH2-CH:CH-NO2, a modestly diastereoselective transformation. A more practical second-generation synthetic route was developed that is based on a novel method for the asym. synthesis of organofluorine compds., by enolate alkylation using optically active fluoroiodoacetic acid as the electrophile in combination with a chiral amide enolate. Resolution of fluoroiodoacetic acid with ephedrine provides either enantiomeric form of the electrophile in ≥96% ee. Alkylation reactions with this stable and storable chiral fluorinated precursor are shown to proceed in a highly stereospecific manner. With the development of substrate-controlled syn- or anti-selective redns. of α-fluoro ketones (I; F, CH2Ph trans and I; F, CH2Ph = cis; diastereomeric ratios 12:1-84:1), efficient and stereoselective routes to each of the four targeted inhibitors were achieved. The optimized synthetic route to the most potent inhibitor (II; Ki = 2.0 nM) proceeded in seven steps (87% average yield per step) from aminoindanol hydrocinnamide and (S)-fluoroiodoacetic acid, and allowed for the preparation of more than 1 g of this compound The inhibition of HIV-1 protease by each of the fluorinated inhibitors was evaluated in vitro, and the variation of potency as a function of inhibitor stereochem. is discussed.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
ST fluoroacetamide nitroalkene diastereoselective conjugate addn prepn HIV1 protease inhibitors; asym alkylation fluoroiodoacetate amide enolate prepn HIV1 protease inhibitors; fluoro ketone prepn HIV1 protease inhibitors
IT Addition reaction
(conjugate; preparation of monofluoro hydroxyethylene dipeptide isosteres as HIV-1 protease inhibitors)
IT Ketones, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(fluoro; preparation of monofluoro hydroxyethylene dipeptide isosteres as HIV-1 protease inhibitors)
IT Human immunodeficiency virus 1
Resolution (separation)
(preparation of monofluoro hydroxyethylene dipeptide isosteres as HIV-1 protease inhibitors)
IT Alkylation
(stereoselective; preparation of monofluoro hydroxyethylene

dipeptide isosteres as HIV-1 protease inhibitors)
IT 360558-30-1P 360558-32-3P 360558-54-9P 360558-55-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of monofluoro hydroxyethylene dipeptide isosteres as HIV-1 protease inhibitors)
IT 79-37-8, Oxalyl chloride 116-11-0 123-38-6, Propionaldehyde, reactions 359-06-8, Fluoroacetyl chloride 401-55-8, Ethyl bromofluoroacetate 500-22-1, 3-Pyridinecarboxaldehyde 593-71-5, Chloroiodomethane 2230-82-2 6959-48-4, 3-Picolyl chloride, hydrochloride 10147-11-2, 3-Phenyl-1-propyne 14980-86-0 49676-93-9 62634-65-5 126456-43-7 141018-37-3 150323-35-6 150378-17-9, Indinavir 204323-36-4 360558-15-2 360558-27-6 360558-81-2 360558-82-3 454421-36-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of monofluoro hydroxyethylene dipeptide isosteres as HIV-1 protease inhibitors)
IT 401-58-1P 471-45-4P 113361-26-5P 138775-03-8P 150407-68-4P 172820-50-7P 185213-44-9P 205251-13-4P 329259-23-6P 329259-25-8P 329259-27-0P 329259-29-2P 329259-31-6P 360558-16-3P 360558-17-4P 360558-18-5P 360558-19-6P 360558-20-9P 360558-22-1P 360558-23-2P 360558-24-3P 360558-25-4P 360558-26-5P 360558-28-7P 360558-29-8P 360558-31-2P 360558-33-4P 360558-34-5P 360558-35-6P 360558-36-7P 360558-37-8P 360558-38-9P 360558-39-0P 360558-40-3P 360558-41-4P 360558-42-5P 360558-43-6P 360558-44-7P 360558-45-8P 360558-46-9P 360558-47-0P 360558-48-1P 360558-49-2P 360558-50-5P 360558-51-6P 360558-52-7P 360558-53-8P 360558-56-1P 360558-58-3P 360558-59-4P 360558-60-7P 360558-61-8P 360558-62-9P 360558-63-0P 360558-64-1P 360558-65-2P 360558-66-3P 360558-67-4P 360558-68-5P 360558-69-6P 360558-70-9P 360558-71-0P 360558-72-1P 360558-73-2P 360558-75-4P 360558-76-5P 360558-77-6P 360562-74-9P
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(preparation of monofluoro hydroxyethylene dipeptide isosteres as HIV-1 protease inhibitors)
IT 360558-21-0P 360558-57-2P 360558-74-3P 360558-78-7P 360558-79-8P 360558-80-1P 360558-83-4P 360558-84-5P 360558-85-6P 360558-86-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of monofluoro hydroxyethylene dipeptide isosteres as HIV-1 protease inhibitors)
REFERENCE COUNT: 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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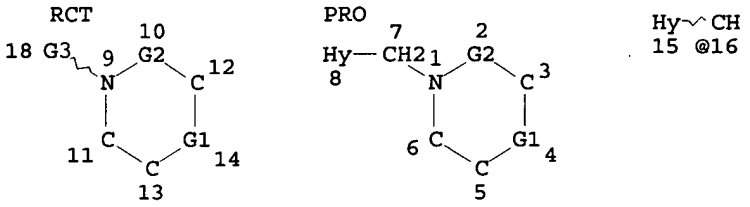


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STEREO ATTRIBUTES: NONE

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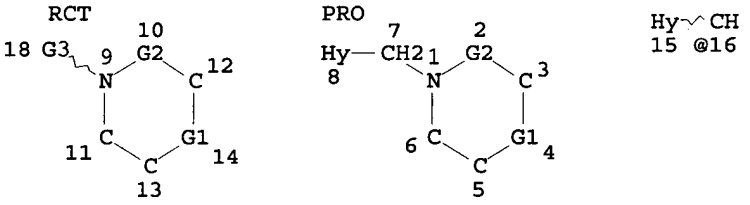


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STEREO ATTRIBUTES: NONE

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PRO
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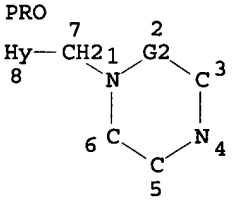


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NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
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L42             SCR 1994
L43             SCR 1607
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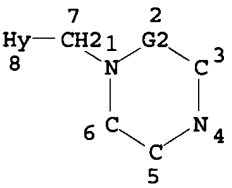


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GGCAT   IS UNS  AT   8
DEFAULT ECLEVEL IS LIMITED
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ECOUNT IS M1 C M1 N AT 8

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE

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L112 ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:1021624  HCAPLUS
DOCUMENT NUMBER:         143:326392
TITLE:                   Preparation of biaryl amines as M3 muscarinic
                         acetylcholine receptor antagonists
INVENTOR(S):             Budzik, Brian W.; Cooper, Anthony W. J.;
                         Corbett, David Francis; Jin, Jian; Laine,
                         Dramane I.; Wang, Yonghui; Moore, Michael Lee;
                         Rivero, Ralph A.; Shi, Dongchuan; Wang, Feng;
                         Xie, Haibo; Zhu, Chongjie
PATENT ASSIGNEE(S):      Glaxo Group Limited, UK; et al.
SOURCE:                  PCT Int. Appl., 101 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
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             LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                       US 2004-552106P     P
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OTHER SOURCE(S):         MARPAT 143:326392
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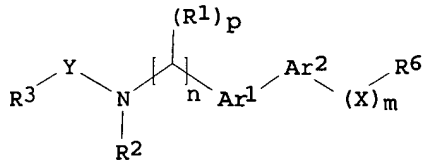

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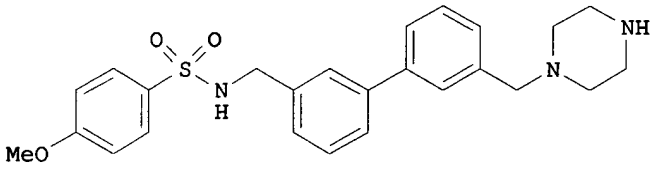

II

AB Title compds. I [wherein Ar1, Ar2 = (un)substituted Ph or monocyclic heteroaryl; R6 = (un)substituted amine; X = C(R1)p when m = 0-3; X = CO when m = 1; p = 0-2; n = 0-3; Y = CO, SO, SO2, HNC(O) or OC(O); R1, R2 = H, (un)substituted alkyl, etc.; R3 = (un)substituted (hetero)aryl, etc., or pharmaceutically acceptable salts thereof] were prepared as M3 muscarinic acetylcholine receptor antagonists. For instance, solid-phase synthesis of II·2CF3COOH was realized in an overall yield of 46% on 2,6-dimethoxy-4-polystyrenebenzyloxybenzaldehyde (DMHB resin), via (1) reductive amination with 3-bromobenzylamine hydrochloride; (2) N-sulfonation with 4-methoxybenzenesulfonyl chloride; (3) Pd-**catalyzed** coupling with 3-formylphenylboronic acid; (4) reductive amination with N-Bocpiperazine; and (5) cleavage from the resin with TFA. No biol. data were given. I and pharmaceutical compns. are potentially useful for the treatment of muscarinic acetylcholine receptor-mediated diseases, such as respiratory tract disorders.

IT **865312-59-0P 865312-62-5P 865312-64-7P 865313-97-9P 865314-01-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antagonist; preparation of biaryl amines as M3 muscarinic acetylcholine receptor antagonists)

RN 865312-59-0 HCAPLUS

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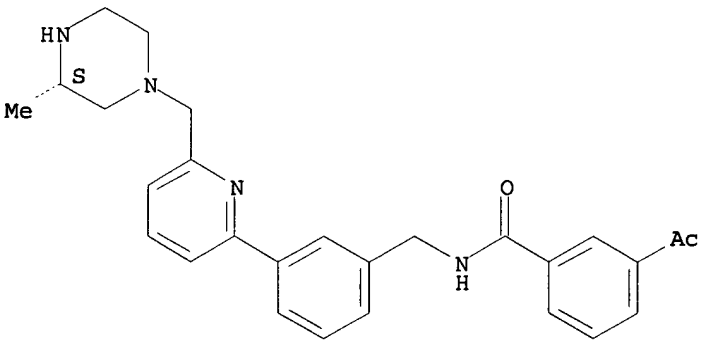
Absolute stereochemistry.

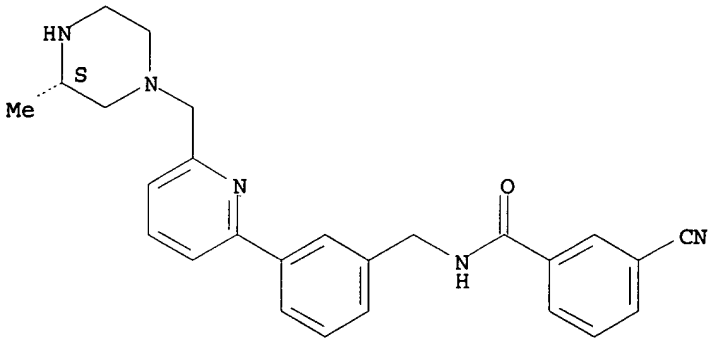


RN 865312-62-5 HCAPLUS

CN Benzamide, 3-cyano-N-[[3-[6-[[(3S)-3-methyl-1-piperazinyl]methyl]-

2-pyridinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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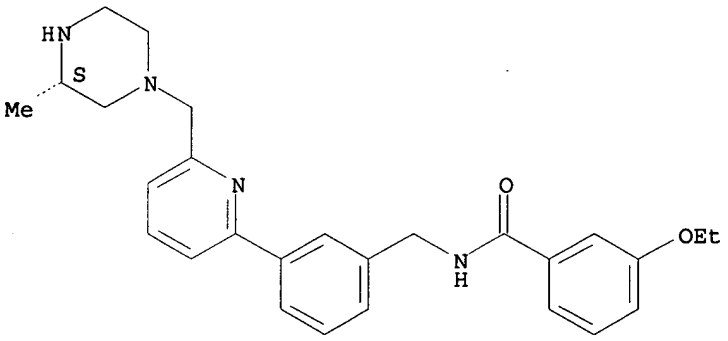
CN Benzamide, 3-ethoxy-N-[[3-[6-[[(3S)-3-methyl-1-piperazinyl]methyl]-2-pyridinyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 865313-97-9 HCAPLUS
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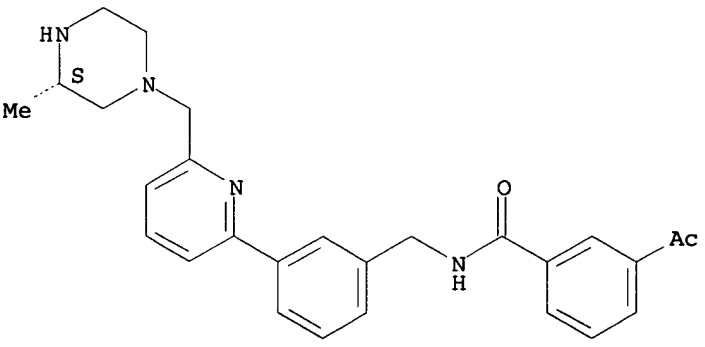
CMF C27 H30 N4 O2

Absolute stereochemistry.



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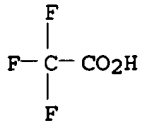
CMF C2 H F3 O2

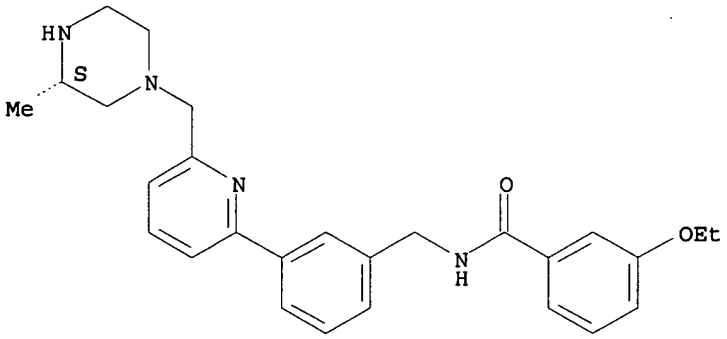


RN 865314-01-8 HCAPLUS
CN Benzamide, 3-ethoxy-N-[[3-[6-[[(3S)-3-methyl-1-piperazinyl]methyl]-2-pyridinyl]phenyl]methyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 865312-64-7
CMF C27 H32 N4 O2

Absolute stereochemistry.



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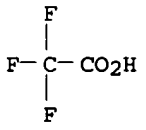
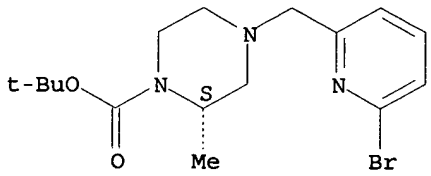


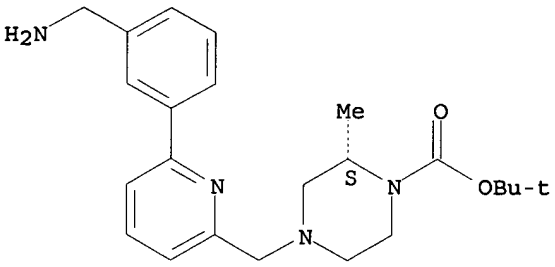
IT **865314-25-6P 865314-26-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of biaryl amines as M3 muscarinic acetylcholine receptor antagonists)
RN 865314-25-6 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(6-bromo-2-pyridinyl)methyl]-2-methyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 865314-26-7 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[6-[3-(aminomethyl)phenyl]-2-pyridinyl]methyl]-2-methyl-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-495
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CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 25, 63
IT 865311-83-7P 865311-84-8P 865311-85-9P 865311-86-0P
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865315-39-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antagonist; preparation of biaryl amines as M3 muscarinic acetylcholine receptor antagonists)

IT 94-53-1, Piperonylic acid 98-68-0, 4-Methoxybenzenesulfonyl chloride 98-88-4, Benzoyl chloride 111-64-8, Octanoyl chloride 121-43-7, Trimethyl **borate** 579-18-0 586-42-5, 3-Acetylbenzoic acid 621-51-2 636-76-0, 3-(Aminosulfonyl)benzoic acid 765-30-0, Cyclopropylamine 823-78-9, 3-Bromobenzyl bromide 1877-72-1, 3-Cyanobenzoic acid 3132-99-8, 3-Bromobenzaldehyde 3201-54-5 4314-22-1, 1H-1,2,3-Triazole-1-acetic acid 4701-17-1, 5-Bromo-2-thiophenecarboxaldehyde 6952-59-6, 3-Bromobenzonitrile 25487-66-5 38628-51-2 39959-54-1, 3-Bromobenzylamine hydrochloride 57260-71-6, 1,1-Dimethylethyl 1-piperazinecarboxylate 72235-56-4, 3-Chloro-4-fluorobenzylamine 74879-18-8, (S)-2-Methylpiperazine 87199-16-4, 3-Formylphenylboronic acid 127972-02-5, (5-Formyl-2-methoxyphenyl)boronic acid 169447-70-5 202865-68-7 214210-21-6, (3-Cyano-4-fluorophenyl)boronic acid 352525-94-1, [3-(Aminomethyl)phenyl]boronic acid hydrochloride 865314-17-6 865314-20-1 865314-31-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of biaryl amines as M3 muscarinic acetylcholine receptor antagonists)

IT 10269-01-9DP, 3-Bromobenzylamine, DMHB resin-bound 60031-08-5P 423154-81-8P 865314-18-7P 865314-19-8P 865314-21-2P 865314-22-3P 865314-23-4P 865314-24-5P **865314-25-6P** **865314-26-7P** 865314-27-8P 865314-28-9P 865314-29-0P 865314-30-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of biaryl amines as M3 muscarinic acetylcholine receptor antagonists)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L112 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:141200 HCAPLUS
DOCUMENT NUMBER: 142:254568
TITLE: Methods and compositions for increasing the efficacy of biologically-active ingredients such as antitumor agents
INVENTOR(S): Windsor, J. Brian; Roux, Stan J.; Lloyd, Alan M.; Thomas, Collin E.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 243 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014777	A2	20050217	WO 2003-US32667	20031016
WO 2005014777	A3	20050915		
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PRIORITY APPLN. INFO.:	US 2002-418803P	P	20021016
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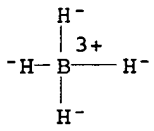
AB The invention provides methods and compns. for modulating the sensitivity of cells to cytotoxic compds. and other active agents. In accordance with the invention, compns. are provided comprising combinations of ectophosphatase inhibitors and active agents. Active agents include antibiotics, fungicides, herbicides, insecticides, chemotherapeutic agents, and plant growth regulators. By increasing the efficacy of active agents, the invention allows use of compns. with lowered concns. of active ingredients.

IT **16940-66-2 138261-41-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for increasing efficacy of biol. active ingredients such as antitumor agents)

RN 16940-66-2 HCAPLUS
CN Borate(1-), tetrahydro-, sodium (8CI, 9CI) (CA INDEX NAME)



RN 138261-41-3 HCAPLUS
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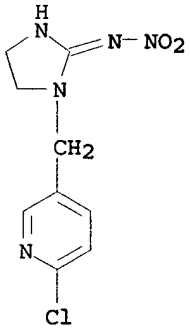

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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(methods and compns. for increasing efficacy of biol. active
ingredients such as antitumor agents)

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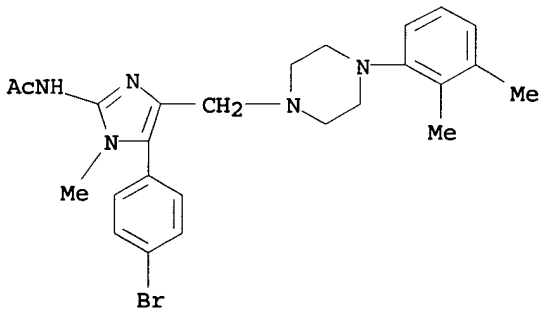
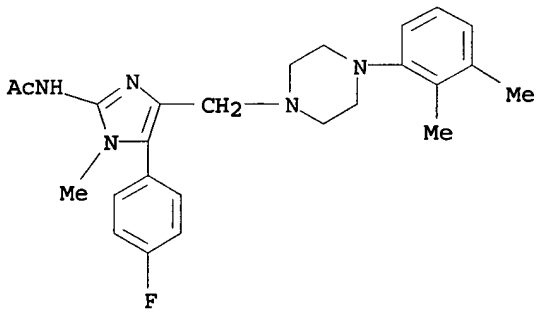
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for increasing efficacy of biol. active ingredients such as antitumor agents)

L112 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:153240 HCAPLUS
DOCUMENT NUMBER: 141:395471
TITLE: Method for preparation of 1-methyl-5-aryl-2-aminoimidazoles and their reactivity
AUTHOR(S): Smirnova, T. A.; Kurapov, P. B.; Vetrova, E. L.; Bass, A. G.; Nam, N. L.
CORPORATE SOURCE: Kafedra Org. Khim., Timiryazevsk. S-Kh. Akad., Russia
SOURCE: Izvestiya Timiryazevskoi Sel'skokhozyaistvennoi Akademii (2003), (4), 132-141
CODEN: ITSAA7; ISSN: 0021-342X
PUBLISHER: ANO "Izdatel'stvo MSKhA"
DOCUMENT TYPE: Journal
LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 141:395471
AB In search for novel compds. with plant growth regulation activity, a series of 1-methyl-5-aryl-2-aminoimidazoles were synthesized in 5 steps from 2-aminopyrimidine and substituted α-bromoacetophenones. The products were further functionalized by acylation with acid chlorides or anhydrides, reductive coupling with aldehydes, Mannich reaction or cyclocondensation with α-bromoacetophenones.
IT **787586-99-6P 787587-00-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (methyl)(aryl)aminoimidazoles from aminopyrimidine and their acylation with acid chlorides and anhydrides, Mannich reactions, reductive coupling with aldehydes and cyclocondensation with α-bromoacetophenones)
RN 787586-99-6 HCAPLUS
CN Acetamide, N-[5-(4-bromophenyl)-4-[[4-(2,3-dimethylphenyl)-1-piperazinyl]methyl]-1-methyl-1H-imidazol-2-yl]- (9CI) (CA INDEX NAME)



RN 787587-00-2 HCAPLUS
CN Acetamide, N-[4-[[4-(2,3-dimethylphenyl)-1-piperazinyl]methyl]-5-(4-fluorophenyl)-1-methyl-1H-imidazol-2-yl]- (9CI) (CA INDEX NAME)



CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
IT **Aldehydes, reactions**
RL: RCT (Reactant); **RACT (Reactant or reagent)**
(aromatic; preparation of (methyl)(aryl)aminoimidazoles from aminopyrimidine and their acylation with acid chlorides and anhydrides, Mannich reactions, reductive coupling with aldehydes and cyclocondensation with α-bromoacetophenones)

IT 405141-01-7P 736960-76-2P 736969-33-8P 736973-92-5P
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RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of (methyl)(aryl)aminoimidazoles from aminopyrimidine and their acylation with acid chlorides and anhydrides, Mannich reactions, reductive coupling with aldehydes and cyclocondensation with α-bromoacetophenones)

L112 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:695680 HCAPLUS
DOCUMENT NUMBER: 137:228094
TITLE: Termiticidal baits for eliminating termite colonies
INVENTOR(S): Brode, Philip Frederick, III; Garrett, Garry Steven; Laughlin, Leo Timothy; Matthews, Randall Stryker; Barker, Dale Edwin; Kinne, Daniel James; Miller, Christopher Miles; Probst, Timothy Robert; McKibben, Gary Eugene
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002069704        A2    20020912    WO 2002-US6200
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OTHER SOURCE(S): MARPAT 137:228094

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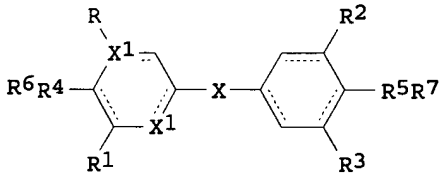


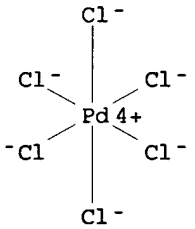
I

AB This invention relates to devices, kits, and methods for eliminating termite colonies. The kits, devices, and methods employ a termiticidal bait matrix contain (a) a termiticide (I, X = nil, a hydrocarbon group, O or NR8,R9 where R8 and R9 are H or a hydrocarbon group; X1 = CH, a carbon atom or a heteroatom; R,R1,R2,R3 = H or OH and if R4 and R5 are O and R6 and R7 are H then R,R1,R2 and R3 may be C1-6; R4 and R5 are H, O or N; R9 and R10 are nil, C1-6, and amides) selected such that the termiticide causes death to about 50 to about 100% of termites within about 24 to about 84 days after the termites begin to ingest the termiticide or the bait matrix comprising the termiticide, (b) a cellulose containing material, and (c) water. The termiticidal bait matrix can be used in a bait station installed in the ground. The kits are suitable to be used by consumers in their homes.

IT **17141-41-2D**, Hexachloropalladate(2-), compds.
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cellulase inhibitor in termiticidal baits for eliminating termite colonies)

RN 17141-41-2 HCAPLUS

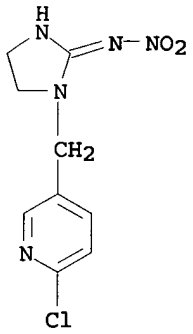
CN Palladate(2-), hexachloro-, (OC-6-11)- (9CI) (CA INDEX NAME)



IT **138261-41-3**, Imidacloprid
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(slow-acting toxicant in termiticidal baits for eliminating termite colonies)

RN 138261-41-3 HCAPLUS

CN 2-Imidazolidinimine, 1-[(6-chloro-3-pyridinyl)methyl]-N-nitro- (9CI) (CA INDEX NAME)



IC ICM A01N025-02

CC 5-4 (Agrochemical Bioregulators)
Section cross-reference(s): 43

IT 80-04-6 80-05-7, biological studies 128-08-5 1752-96-1 2226-96-2 3363-56-2 3377-24-0, Cyclohexanamine, 4,4'-(1-methylethylidene)bis- 3576-88-3 4199-10-4 5437-98-9 5613-46-7 10041-06-2 10192-62-8 14090-83-6

17141-41-2D, Hexachloropalladate(2-), compds. 19168-23-1
28230-32-2 32212-38-7 34211-05-7 50541-93-0 62220-58-0
65252-01-9 85803-43-6 154862-23-4 176674-53-6 195052-64-3
213193-76-1 300820-15-9 300822-69-9 312514-22-0
325154-80-1 345257-94-5 347909-13-1 413612-51-8
415694-09-6 420820-23-1 424809-13-2 425411-08-1
457066-48-7 457066-50-1 457066-51-2 457066-52-3
457066-53-4 457066-54-5 457066-55-6 457066-56-7
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cellulase inhibitor in termiticidal baits for eliminating termite colonies)

IT 7440-39-3D, Barium, compds. 7440-42-8D, Boron, compds.
11141-17-6, Azadirachtin **138261-41-3**, Imidacloprid
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(slow-acting toxicant in termiticidal baits for eliminating termite colonies)

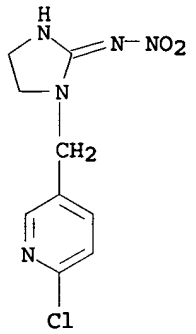
L112 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:493021 HCAPLUS
DOCUMENT NUMBER: 136:243278
TITLE: Field evaluation of non-pesticide chemicals as honey bee repellents
AUTHOR(S): Mayer, D. F.; Lunden, J. D.; Kovacs, G.; Miliczky, E. R.
CORPORATE SOURCE: Department of Entomology, Irrigated Agriculture Research & Extension Center, Washington State University, Prosser, WA, 99350, USA
SOURCE: Colloques - Institut National de la Recherche Agronomique (2001), 98(Hazards of Pesticides to Bees), 159-168
CODEN: COLIEZ; ISSN: 0293-1915
PUBLISHER: Institut National de la Recherche Agronomique
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bee poisoning from pesticides is a serious problem worldwide. Major concern exists for the safety of honey bees (Apis mellifera L.) as valuable pollinators of many horticultural crops. One way of reducing the pesticide hazard to bees is to apply a chemical repellent that will discourage bees from foraging on crops for an interval after a bee hazard pesticide has been applied. During 1990-1998, the authors conducted field tests on blooming apples (Malus domestica Borkh.), dandelions (Taraxacum officinale G. Weber, in Wiggers), buckwheat (officinale) and white Dutch clover (officinale) plants to evaluate their repellent effect to foraging honey bees. Evaluations were made by slowly walking through the plots and counting the number of honey bees (30 s/6.7 m/0.91 m swath) except for apples where they were counted by slowly moving around and counting the number of honey bees (30 s/1 tree) at 1 and 4 h. after application. The authors evaluated about 240 non-pesticide chems. Eleven chems. significantly reduced the number of honey bee foragers at 1 h. after application but not at 4 h. In some tests, but not all, 10 chems. significantly reduced the number of honey bee foragers at 1 h. after application but not at 4 h. One chemical significantly reduced the number of honey bee foragers at 1 h. and 4 h. after application. In some tests, but not all, 2 chems. significantly reduced the number of honey bee foragers at 4 h. after application but not at 1 h.

IT **138261-41-3**, NTN 33893-240FS
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(field evaluation of non-pesticide chems. as honey bee repellents)

RN 138261-41-3 HCAPLUS

CN 2-Imidazolidinimine, 1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-
(9CI) (CA INDEX NAME)



CC 5-4 (Agrochemical Bioregulators)
IT Repellents
(**cat** and dog repellents; field evaluation of
non-pesticide chems. as honey bee repellents)
IT 54-12-6, Tryptophan 56-54-2, Quinidine 57-10-3, Palmitic acid,
biological studies 57-11-4, Stearic acid, biological studies
60-24-2, 2-Mercaptoethanol 60-35-5, Acetamide, biological
studies 64-10-8, Phenylurea 64-19-7, Acetic acid, biological
studies 65-30-5 66-25-1, Hexanal 67-63-0, Isopropanol,
biological studies 67-66-3, Chloroform, biological studies
67-68-5, Dimethyl sulfoxide, biological studies 71-23-8,
Propanol, biological studies 71-36-3, 1-Butanol, biological
studies 75-15-0, Carbon disulfide, biological studies 75-50-3,
Trimethylamine, biological studies 75-65-0, 2-Methyl-2-propanol,
biological studies 76-22-2, Camphor 78-70-6, Linalool
78-93-3, 2-Butanone, biological studies 79-16-3,
N-Methylacetamide 79-31-2, Isobutyric acid 79-77-6,
β-Ionone 80-59-1, Tiglic acid 83-34-1, Skatole 84-66-2,
Diethylphthalate 87-44-5 89-83-8, Thymol 90-02-8,
Salicylaldehyde, biological studies 93-58-3, Methyl benzoate
94-96-2 95-48-7, o-Cresol, biological studies 97-53-0, Eugenol
99-03-6, 3'-Aminoacetophenone 99-76-3, p-Hydroxybenzoic acid
methyl ester 100-41-4, Ethyl benzene, biological studies
100-52-7, Benzaldehyde, biological studies 101-31-5,
l-Hyoscyamine 103-83-3, Dimethylbenzylamine 104-75-6,
2-Ethylhexylamine 106-35-4, 3-Heptanone 106-44-5, p-Cresol,
biological studies 106-65-0, Succinic acid dimethyl ester
106-68-3, 3-Octanone 107-06-2, 1,2-Dichloroethane, biological
studies 107-87-9, 2-Pentanone 108-05-4, Vinyl acetate,
biological studies 108-31-6, Maleic anhydride, biological
studies 108-95-2, Phenol, biological studies 110-12-3,
5-Methyl-2-hexanone 110-13-4, 2,5-Hexanedione 110-43-0,
2-Heptanone 110-54-3, n-Hexane, biological studies 110-93-0,
6-Methyl-5-hepten-2-one 111-13-7, 2-Octanone 111-27-3,
1-Hexanol, biological studies 111-84-2, n-Nonane 111-87-5,
1-Octanol, biological studies 112-14-1, Octylacetate 112-17-4,
n-Decylacetate 112-37-8, Undecanoic acid 112-39-0, Palmitic
acid methyl ester 112-44-7, Undecanal 119-61-9, Benzophenone,
biological studies 120-72-9, Indole, biological studies
122-79-2, Phenyl acetate 123-11-5, p-Anisaldehyde, biological
studies 123-19-3, 4-Heptanone 123-72-8, Butyraldehyde
123-92-2, Isoamyl acetate 124-07-2, Caprylic acid, biological
studies 125-12-2, Isobornyl acetate 133-06-2, Captan
135-19-3, β-Naphthol, biological studies 136-45-8, MGK
repellent 326 138-86-3, Limonene 140-11-4, Benzyl acetate
142-62-1, n-Caproic acid, biological studies 142-82-5,
n-Heptane, biological studies 147-85-3, L-Proline, biological

studies 147-93-3, o-Mercaptobenzoic acid 328-50-7, α-Ketoglutaric acid 331-39-5, Caffeic acid 334-48-5, Capric acid 458-37-7, Curcumin 470-82-6, Cineole 471-34-1, Calcium carbonate, biological studies 488-10-8, Jasmone 490-79-9, 2,5-Dihydroxybenzoic acid 499-75-2, Carvacrol 502-49-8, Cyclooctanone 506-12-7, Heptadecanoic acid 507-70-0, Borneol 540-84-1, 2,2,4-Trimethylpentane 544-63-8, Tetradecanoic acid, biological studies 546-49-6, Artemisia ketone 551-93-9, 2'-Aminoacetophenone 614-18-6, Ethyl nicotinate 624-92-0, Methyldisulfide 629-19-6, n-Propyl disulfide 638-53-9, Tridecanoic acid 705-86-2, δ-Decalactone 941-98-0, 1'-Acetonaphthone 1330-43-4, Sodium **tetraborate** 1337-83-3, Aldenal C 11 1596-84-5, Succinic acid 2,2-dimethylhydrazide 2016-57-1, Decylamine 2039-88-5, 2-Bromostyrene 2186-92-7, Anisaldehyde dimethylacetal 2315-68-6, n-Propyl benzoate 3391-86-4, 1-Octen-3-ol 3796-70-1, Geranylacetone 4602-84-0, Farnesol 7620-46-4, 9-Isothiocyanato acridine 7664-38-2, Phosphoric acid, biological studies 7704-34-9, Microthiol, biological studies 9004-99-3 12240-15-2, Prussian Blue 14371-10-9, trans-Cinnamaldehyde 20244-19-3 23422-53-9, Carzol 92SP 24804-31-7, Calcium oxalate hydrate 25414-22-6, 2-Methoxyfuran 27941-88-4, Amino acetophenone 36653-82-4, 1-Hexadecanol 41446-60-0, cis-7-Tetradecene 62242-52-8, Hexadecanone 70802-40-3 74214-63-4, β-Carboline-3-carboxylic acid 90823-38-4, Ro-Pel 116580-64-4, Margosan O **138261-41-3** , NTN 33893-240FS 143350-75-8, Kinetic 404578-56-9, Algafer LPF 404580-56-9, Baitmate 404580-58-1, Can 17 404580-65-0, Compensol 404580-79-6, N-O-Dor II 404581-66-4, AeroSpray 404582-04-3, Epoleon N 100 404582-84-9, Scent-A-Way 404582-85-0, Sun Shield 404582-89-4, Terramark SPI 404582-90-7, Super Pepper Guard 404582-91-8, Free Shield 404582-94-1, Frost Shield 404583-18-2, Fruit Boost (insect attractant) 404583-20-6, Nutra-sol 404584-91-4, Get Off My Garden 404585-84-8, Uran 32 404586-91-0, X-O Deodorizer 404586-92-1, XP 201 404586-93-2, Y-Guard 404587-06-0, U-V-Killer
RL: AGR (Agricultural use); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(field evaluation of non-pesticide chems. as honey bee repellents)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

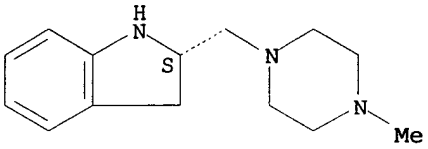
L112 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:50021 HCAPLUS
DOCUMENT NUMBER: 130:182220
TITLE: Enantioselective addition of dialkylzinc to aldehydes catalyzed by (S)-2-(N,N-disubstituted aminomethyl)indoline
AUTHOR(S): Asami, Masatoshi; Watanabe, Hiroyasu; Honda, Kiyoshi; Inoue, Seiichi
CORPORATE SOURCE: Department of Synthetic Chemistry, Faculty of Engineering, Yokohama National University, Tokiwadai, Hodogaya-ku, Yokohama, 240-8501, Japan
SOURCE: Tetrahedron: Asymmetry (1998), 9(23), 4165-4173
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:182220
AB Chiral di- or tri-amines, (S)-2-(N,N-disubstituted aminomethyl)indoline, derived from (S)-indoline-2-carboxylic acid

were efficient chiral catalysts for the enantioselective addition of dialkylzincs to aldehydes. The best results were obtained by employing 15 mol% of (S)-2-(4-methyl-1-piperazinylmethyl)indoline, and chiral secondary alcs. were obtained in up to 97% ee.

IT **220648-71-5P 220648-72-6P**
RL: CAT (Catalyst use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(preparation of chiral (aminomethyl)indole derivs. as catalysts for addition of dialkylzinc to aldehydes)

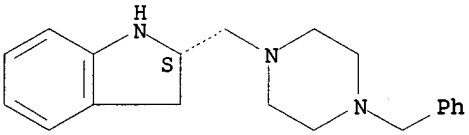
RN 220648-71-5 HCAPLUS
CN 1H-Indole, 2,3-dihydro-2-[(4-methyl-1-piperazinyl)methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 220648-72-6 HCAPLUS
CN 1H-Indole, 2,3-dihydro-2-[[4-(phenylmethyl)-1-piperazinyl]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



CC 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

IT **Aldehydes, reactions**
RL: RCT (Reactant); **RACT (Reactant or reagent)**
(aromatic; preparation of chiral (aminomethyl)indole derivs. as catalysts for addition of dialkylzinc to aldehydes)

IT **Aldehydes, reactions**
RL: RCT (Reactant); **RACT (Reactant or reagent)**
(preparation of chiral (aminomethyl)indole derivs. as catalysts for addition of dialkylzinc to aldehydes)

IT 198218-48-3P 220648-69-1P 220648-70-4P **220648-71-5P**
220648-72-6P
RL: CAT (Catalyst use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(preparation of chiral (aminomethyl)indole derivs. as catalysts for addition of dialkylzinc to aldehydes)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

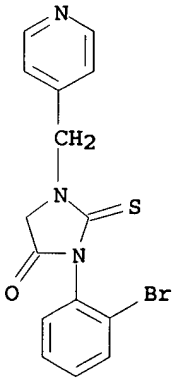
L112 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:281207 HCAPLUS
DOCUMENT NUMBER: 127:5044
TITLE: Solution-Phase Synthesis of a Combinatorial Thiohydantoin Library
AUTHOR(S): Sim, Mui Mui; Ganesan, Arasu
CORPORATE SOURCE: Institute of Molecular and Cell Biology, National University of Singapore, 119260, Singapore
SOURCE: Journal of Organic Chemistry (1997), 62(10), 3230-3235

CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:5044

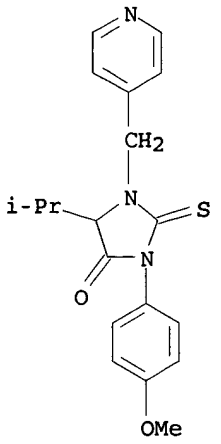
AB An efficient one-pot three-component synthesis of thiohydantoins was developed. In the first step, amino acid esters were alkylated by imine formation with aldehydes and reduction by sodium triacetoxyborohydride. In the second step, an isothiocyanate was added together with a molar equivalent of triethylamine, leading to the thiohydantoin product in high yield and purity after an extractive aqueous workup. This procedure was used to generate a combinatorial library of over 600 discrete thiohydantoins on a 0.1 mmol scale. Sampling of 10% of this library showed the thiohydantoin to be the major product in all cases, with purities of 52-98% by HPLC anal. The cyclization conditions can also be adapted to the synthesis of hydantoins.

IT **189948-22-9P 189948-26-3P 189948-28-5P**
189948-30-9P 189948-34-3P 189948-48-9P
189948-54-7P 189948-81-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solution-phase synthesis of a combinatorial thiohydantoin library)

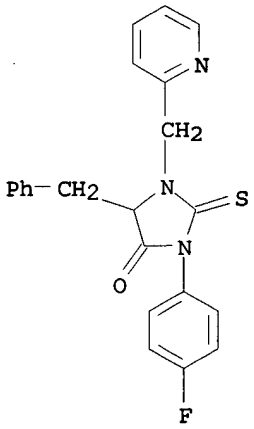
RN 189948-22-9 HCAPLUS
CN 4-Imidazolidinone, 3-(2-bromophenyl)-1-(4-pyridinylmethyl)-2-thioxo- (9CI) (CA INDEX NAME)



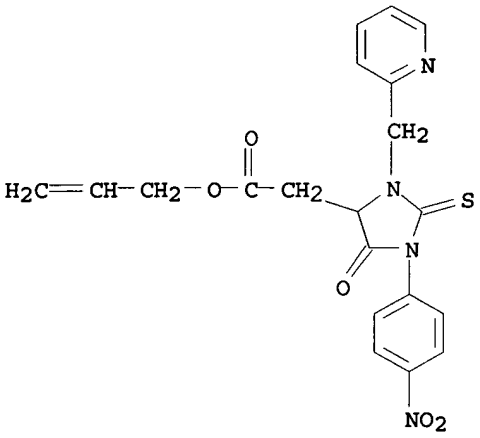
RN 189948-26-3 HCAPLUS
CN 4-Imidazolidinone, 3-(4-methoxyphenyl)-5-(1-methylethyl)-1-(4-pyridinylmethyl)-2-thioxo- (9CI) (CA INDEX NAME)



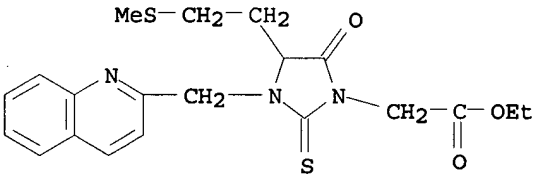
RN 189948-28-5 HCAPLUS
CN 4-Imidazolidinone, 3-(4-fluorophenyl)-5-(phenylmethyl)-1-(2-pyridinylmethyl)-2-thioxo- (9CI) (CA INDEX NAME)



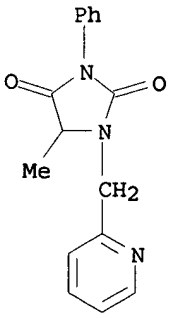
RN 189948-30-9 HCAPLUS
CN 4-Imidazolidineacetic acid, 1-(4-nitrophenyl)-5-oxo-3-(2-pyridinylmethyl)-2-thioxo-, 2-propenyl ester (9CI) (CA INDEX NAME)



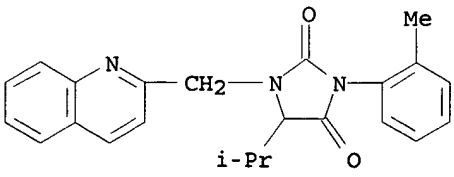
RN 189948-34-3 HCAPLUS
CN 1-Imidazolidineacetic acid, 4-[2-(methylthio)ethyl]-5-oxo-3-(2-quinolinylmethyl)-2-thioxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 189948-48-9 HCAPLUS
CN 2,4-Imidazolidinedione, 5-methyl-3-phenyl-1-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)

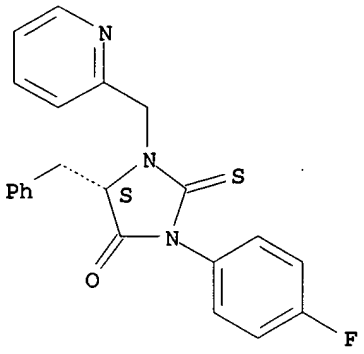


RN 189948-54-7 HCAPLUS
CN 2,4-Imidazolidinedione, 5-(1-methylethyl)-3-(2-methylphenyl)-1-(2-quinolinylmethyl)- (9CI) (CA INDEX NAME)



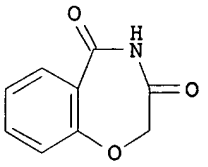
RN 189948-81-0 HCAPLUS
CN 4-Imidazolidinone, 3-(4-fluorophenyl)-5-(phenylmethyl)-1-(2-pyridinylmethyl)-2-thioxo-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
IT **Aldehydes, reactions**
RL: RCT (Reactant); **RACT (Reactant or reagent)**
(aromatic; solution-phase synthesis of a combinatorial thiohydantoin library)
IT 83800-58-2P 189948-21-8P **189948-22-9P** 189948-23-0P
189948-24-1P 189948-25-2P **189948-26-3P** 189948-27-4P
189948-28-5P 189948-29-6P **189948-30-9P**
189948-31-0P 189948-32-1P 189948-33-2P **189948-34-3P**
189948-35-4P 189948-37-6P 189948-38-7P 189948-39-8P
189948-41-2P 189948-43-4P 189948-46-7P **189948-48-9P**
189948-50-3P 189948-52-5P **189948-54-7P** 189948-56-9P
189948-58-1P 189948-59-2P 189948-61-6P 189948-62-7P
189948-64-9P 189948-65-0P 189948-67-2P 189948-69-4P
189948-71-8P 189948-73-0P 189948-75-2P 189948-77-4P
189948-79-6P **189948-81-0P** 189948-82-1P 189948-83-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solution-phase synthesis of a combinatorial thiohydantoin library)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L112 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:211417 HCAPLUS
DOCUMENT NUMBER: 126:251146
TITLE: Synthesis of 1,4-benzoxazepine-3,5-diones as anticonvulsant agents
AUTHOR(S): Youssef, Khairia M.; Said, Makarem M.
CORPORATE SOURCE: Dep. Organic Chem., Cairo Univ., Cairo, Egypt
SOURCE: Egyptian Journal of Pharmaceutical Sciences (1996), 37(1-6), 45-55
CODEN: EJPSBZ; ISSN: 0301-5068
PUBLISHER: National Information and Documentation Centre
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



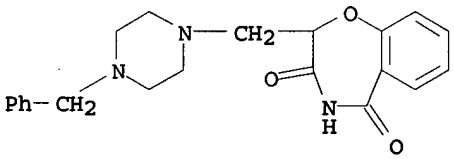
I

AB 1,4-Benzoxazepine-3,5-dione (I) was prepared from (2-carbamoylphenoxy)acetic acid. Mannich reactions of I gave 2-(aminomethyl) derivs.; condensation of I with aromatic aldehydes gave 2-benzylidene derivs. Preliminary anticonvulsant testing of selected products was carried out.

IT **188636-03-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anticonvulsant activity of)

RN 188636-03-5 HCAPLUS

CN 1,4-Benzoxazepine-3,5(2H,4H)-dione, 2-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



CC 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT **Aldehydes, reactions**
RL: RCT (Reactant); **RACT (Reactant or reagent)**
(aromatic; condensation with 1,4-benzoxazepine-3,5-dione)

IT 188635-99-6P 188636-00-2P 188636-02-4P **188636-03-5P**
188636-04-6P 188636-05-7P 188636-06-8P 188636-08-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and anticonvulsant activity of)

L112 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:298553 HCAPLUS
DOCUMENT NUMBER: 125:86673
TITLE: Improved synthesis of an HIV protease inhibitor by reductive amination with pyridinecarboxaldehyde
INVENTOR(S): Askin, David; Cianciosi, Steven J.; Hoerrner, Robert S.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5508404	A	19960416	US 1995-404776	1995

0315

WO 9628440 A1 19960919 WO 1996-US2646
1996
0311

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9651751 A1 19961002 AU 1996-51751
1996
0311

BR 9607374 A 19971230 BR 1996-7374
1996
0311

EP 815102 A1 19980107 EP 1996-908541
1996
0311

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

CN 1183780 A 19980603 CN 1996-193740
1996
0311

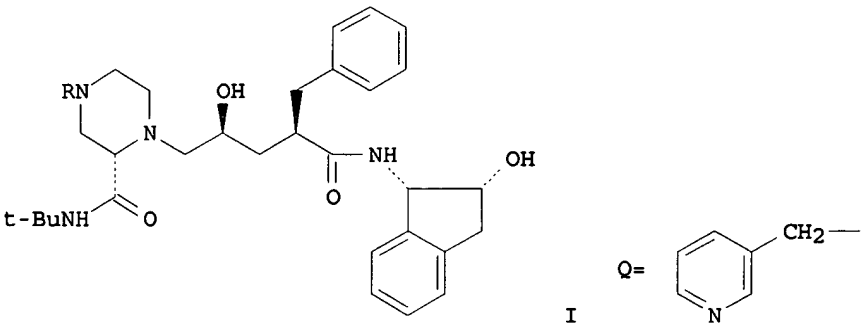
CZ 291035 B6 20021211 CZ 1997-2864
1996
0311

PRIORITY APPLN. INFO.: US 1995-404776 A
1995
0315

WO 1996-US2646 W
1996
0311

OTHER SOURCE(S): CASREACT 125:86673

GI



I

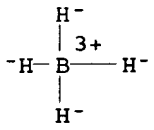
AB A process of reductive amination efficiently yields a known oligopeptide analog (HIV protease inhibitor), namely N-[2(R)-hydroxy-1(S)-indanyl]-2(R)-phenylmethyl-4(S)-hydroxy-5-[1-[4-(3-pyridylmethyl)-2(S)-(N'-tert-butylcarboxamido)piperazinyl]]pentanamide (I; R = Q), which involves reacting for at least 5 min in suitable solvent one equivalent of I (R = H) with excess 3-pyridinecarboxaldehyde in the presence of excess reducing agent at .apprx.-78° to .apprx.90°. The reducing agent is

selected from NaBH4, NaBH3CN, NaBH(OAc)3, Zn/HCl, Fe(CO)5/KOH-EtOH, formic acid, and selenophenol. Thus, 1.00 g I (R = H) (preparation given) was dissolved in 20 mL ClCH2CH2Cl, treated with 310 mg 3-pyridinecarboxaldehyde and 600 mg NaBH(OAc)3, and the resulting mixture was stirred at 21° for 1.25 h to give the title compound I (R = Q) of >99.3% in 88% yield.

IT **16940-66-2**, Sodium borohydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(improved synthesis of an HIV protease inhibitor by reductive amination with pyridinecarboxaldehyde)

RN 16940-66-2 HCAPLUS

CN Borate(1-), tetrahydro-, sodium (8CI, 9CI) (CA INDEX NAME)

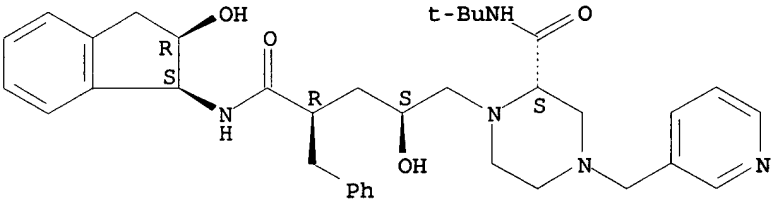


IT **150378-17-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(improved synthesis of an HIV protease inhibitor by reductive amination with pyridinecarboxaldehyde)

RN 150378-17-9 HCAPLUS

CN D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-pyridinylmethyl)-1-piperazinyl]-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07D401-06
INCL 544365000
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 34

IT 64-18-6, Formic acid, reactions 75-05-8, Acetonitrile, reactions 75-64-9, tert-Butylamine, reactions 100-47-0, Benzonitrile, reactions 106-95-6, Allyl bromide, reactions 116-11-0 500-22-1, 3-Pyridinecarboxaldehyde 645-45-4, 3-Phenylpropionyl chloride 645-96-5, Selenophenol 768-22-9, Indene oxide 4377-33-7, Picolyl chloride 7440-66-6, Zinc, reactions 13463-40-6, Iron pentacarbonyl **16940-66-2**, Sodium borohydride 24424-99-5, Di-tert-butyl dicarbonate 25895-60-7, Sodium cyanoborohydride 56553-60-7, Sodium triacetoxyborohydride 114037-15-9, Indandiol
RL: RCT (Reactant); RACT (Reactant or reagent)
(improved synthesis of an HIV protease inhibitor by reductive amination with pyridinecarboxaldehyde)

IT **150378-17-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(improved synthesis of an HIV protease inhibitor by reductive amination with pyridinecarboxaldehyde)

L112 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1964:52796 HCAPLUS
DOCUMENT NUMBER: 60:52796
ORIGINAL REFERENCE NO.: 60:9293g-h,9294a-h,9295a-h,9296a-b
TITLE: Indolylpiperazines
PATENT ASSIGNEE(S): Sterling Drug Inc.
SOURCE: 41 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 944443		19631211	GB	
US 3188313		19650608	US 1959-842203	19590925
PRIORITY APPLN. INFO.:			US	19590925

GI For diagram(s), see printed CA Issue.
AB Compds. of type I and II, in which R1 is H, halogen, alkyl, alkoxy, or aryl, R2 is H, alkyl, hydroxyalkyl, or aryl, R3 and R4 is H, alkyl, or aryl, n is 1 to 7, and in which the indole group may be joined in the 2-position or (as shown) the 3-position, were made. These are useful as hypotensive agents, as antinauseants, antipyretics, sedatives, tranquilizers and muscle relaxants; they inhibit apomorphine-induced vomiting, and prolong the narcosis of ether and barbiturates. A solution of 177 g. (PhCH2)2NCH2CH2NHPh, 120 g. ClCH2COCl and 650 m. CHCl3 was refluxed for 5.5 hrs. to yield 190 g. (PhCH2)2NCH2CH2NPhCOCH2Cl, an oil. This was dissolved in EtOCH2CH2OH, the solution refluxed 4 hrs., cooled, diluted with 650 ml. absolute EtOH, 4 g. Pd-C added, and the mixture reduced by H at 50 lb./in.2 to give 1-phenyl-2-piperazinone (VI), m. 100-5° (p-toluenesulfonate m. 220.2-4.6°).
Similarly made from (PhCH2)2NCH2CH2N(4-ClC6H4)(COCH2Cl) (HCl salt m. 161.0-3.8°) was 1-(4-chlorophenyl)-2-piperazinone (HCl salt m. 192.8-4.8°); from 4-benzyl-1-(2,6-dimethylphenyl)-2-piperazinone (HCl salt m. 248.8-64.8°), 1-(2,6-dimethylphenyl)-2-piperazinone (HCl salt m. 224.8-6.0).
The I and II were made by various methods. Method A: A mixture of 5.6 g. 2-(3-indolyl)ethyl bromide (VII), 4.1 g. 1-phenylpiperazine, 2.1 g. NaHCO3, and 30 ml. absolute EtOH was refluxed for 6 hrs. to yield 1.4 g. I (R1 = R3 = R4 = H, R2 = Ph, n = 2), m. 131.6-6.0°. Similarly prepared were these I (R3 = R4 = H, n = 2; R1, R2, and m.p. given): H, 4-ClC6H4, 185.2-6.8°; H, p-tolyl, 147.8-54.8°; 5-MeO, p-tolyl, 108.6-11.0°; H, PhCH:CHCH2, 258.2-63.6°. Also made was 1-[2-(3-indolyl)ethyl]-trans-2,5-dimethylpiperazine, m. 189.2-90.4°, and from VI and VII 1-[2-(3-indolyl)ethyl]-4-phenyl-3-piperazinone, m. 163.2-4.4°. Method B: To a cold solution of 79.2 g. 1-(o-tolyl)piperazine in 500 ml. tetrahydrofuran (VIII) was added 31.2 g. (3-indolyl)glyoxalyl chloride (IX), the white precipitate filtered off, the filtrate evaporated, the residual gum taken up in a warm mixture of 700 ml. H2O, 120 ml. AcOEt and 25 ml. AcOH, and the solid collected, to give 41.5 g. III (R1 = R3 = R4 = H, R2 = o-tolyl) (X). Similarly prepared were these III (R3 = R4 =

H; R1, R2, and m.p. given): H, Me, --; H, HOCH2CH2, --; H, m-tolyl, --; H, 2-MeOC6H4, --; H, 4-MeOC6H4, 243-5°; H, 3,4-ClMeC6H3, 211-14°; 6-MeO, Ph, 205-9°; 6-MeO, o-tolyl, 247-50°; 6-MeO, m-tolyl, 206-8°; 6-MeO, p-tolyl, 196-8°; 6-MeO, 2-MeOC6H4, 246-8°; 6-MeO, 4-MeOC6H4, 205-10°; 5-PhCH2O, p-tolyl, 148-55°; 5-PhCH2O, PhCH2CH2, 135-40°; 5-MeS, Ph, 188-91°; 5-MeS, p-tolyl, 211-13°; 5,6-(CH2O2), Ph, 267-9°; 5,6-(CH2O2), o-tolyl, 214.6-15.8°; 5,6-(CH2O2), m-tolyl, 212-16°; 5,6-(CH2O2), p-tolyl, 266.4-78.4°; 5,6-(CH2O2), 2-MeOCH2CH2, 205-9°; 5,6-(MeO)2, Ph, 256.8-8.8°; 5,6-(MeO)2, o-tolyl, 211-16°; 5,6-(MeO)2, m-tolyl, 231-8°; 5,6-(MeO)2, p-tolyl, --; 5,6-(MeO)2, 2-MeOC6H4, 218-22°; 5,6-(MeO)2, 3-MeOC6H4, 234.4-6.4°; 5 6-(MeO)2, 4-MeOC6H4, 228-36°; 5,6-(MeO)2, 4-MeSC6H4, 236.4-8.2°; 5,6-(EtO)2, Ph, 180.0-1.0°; H, 2-pyridyl, 242-3°; 4-MeO, Ph, --; 5-MeO, Ph, 224-7.5°; 7-MeO, Ph, --; 6-Me, Ph, --; 6-EtO, Ph, 165° (decomposition); 6-MeO, 2-ClC6H4, 125.2-8.8°; 6-MeO, 3-ClC6H4, 214-16°; 6-MeO, 3-MeOC6H4, 211-13°; 6-MeO, 2-EtOC6H4, 180-4°; 6-MeO, 2,6-Me2C6H3, 215-18°; 6-MeO, 5,2-Cl(MeO)C6H3, 208-11°; 5,6-(MeO)2, PhCH2, 210.2-11.8°; 5,6-EtO(MeO), Ph, 215-22°; 5,6-(MeO)2, 2-pyridyl, 249.6-51.6°; 5,6-(OCH2CH2O), Ph, 172.5-8.5°; 5,6-(MeO)2, 2-EtOC6H4, 135-43°; 5,6-(MeO)2, 2,6-Me2C6H3, 253.2-6.2°; 5,6-(CH2O2), 4-MeOC6H4, 257-8°; 5,6-(CH2O2), 2-BuOC6H4, 164-7.5°; 5,6-(EtO)2, 2-MeOC6H4, 185-6.5°; 5,6-(EtO)2, 3-MeOC6H4, 162-5.5°; H, Ph, 224.2-5.6°; H, PhCH2, 174.4-5.6°; 5,6-(MeO)2, 2-ClC6H4, .apprx.214°; 6-Cl, Ph, 270-4°; 6-MeO, 2-pyridyl, 231-3°; 5,6-(MEO)2, 2-BuOC6H4, 171-4°; 5,6-(MeO)2, 2-EtC6H4, 193-8°; 5,6-(MeO)2, 2,5-(MeO)2C6H3, 208-10°; 5,6-(CH2O2), 2-pyridyl, 271-3°; 5,6-(MeO)2, 2-MeSC6H4, 219-21°. Also prepared were these III (R1, R2, R3, R4, and m.p. given): H, Ph, Me, H, --; 5,6-(MeO)2, Ph, Me, H, 163-74°; 5,6-(CH2O2), 4-MeOC6H4, Me, H, 173-266°; 5,6-(CH2O2), Ph, H, Me, 219-19.8°; 5,6-(MeO)2, Ph, H, Me, 215-22°; H, Ph, Me, Me, --; 6-MeO, Ph, Me, H, 218-20°; 6-MeO, Ph, Ph, H, 155-60°; 5,6-(MeO)2, 2-MeOC6H4, Me, H, 211.4-12.6°; 5,6-(MeO)2, o-tolyl, Me, H, 119-22°; 5,6-(MeO)2, m-tolyl, Me, H, 120-2°; 5,6-(MeO)2, 3-MeOC6H4, Me, H, 159-63.5°; 5,6-(CH2O2), 2-MeOC6H4, Me, H, 233-5°; 5,6-(MeO)2, Ph, Et, H, 177-84°; 5,6-(EtO)2, Ph, Me, H, 182-7°. A solution of 41.5 g. X in 250 ml. VIII was added to a suspension of 27 g. LiAlH4 in 300 ml. VIII, and the mixture refluxed 61/2 hrs. to give 28.5 g. I (R1, R3, R4 = H, R2 = o-tolyl n = 2), m. 124.2-6.4°. Similarly prepared were these I (R3 = R4 = H, n = 2; R1, R2, and m.p. given): H, H, 149.8-52.0°; H, Me, -- (di-HCl salt m. 279.0-83.8°); H, HOCH2CH2, -- (di-HCl salt m. 266.8-71.4°); H, m-tolyl, 163.8-6.2°; H, 2-MeOC6H4, 111.4-14.2°; H, 4-MeOC6H4, 129.8-31.6°; H, 3,4-ClMeC6H3, 159.2-60.6°; 6-MeO, Ph, 137.4-9.6°; 6-MeO, o-tolyl, 139.2-41.4°; 6-MeO, m-tolyl, 119.8-23.4°; 6-MeO, p-tolyl, 172.2-3.4°; 6-MeO, 2-MeOC6H4, 98.2-100.2°; 6-MeO, 4-MeOC6H4, 185.6-8.6°; 5-PhCH2O, p-tolyl, 151.4-3.6°; 5-PhCH2O, PhCH2CH2, 121-3°; 5-MeS, Ph, 110.2-11.6°; 5-MeS, p-tolyl, 111-13.6°; 5,6-(CH2O2), Ph, 141.0-3.2°; 5,6-(CH2O2), o-tolyl, 159.2-60.8°; 5,6-(CH2O2), m-tolyl, 130.0-1.4°; 5,6-(CH2O2), p-tolyl, 187.0-8.8°; 5,6-(CH2O2), 2-MeOC6H4, 158.0-9.4°; 5,6-(MeO)2, Ph, 128.4-30.0°; 5,6-(MeO)2, o-tolyl, -- (HCl salt m. 218.4-23.4°); 5,6-(MeO)2, m-tolyl, 118.4-19.6°; 5,6-(MeO)2, p-tolyl, 137.8-9.2°;

5,6-(MeO)2, 2-MeOC6H4, 116.0-16.6°; 5,6-(MeO)2, 3-MeOC6H4, 123.0-4.0°; 5,6-(MeO)2, 4-MeOC6H4, 158.8-64.0°; 5,6-(MeO)2, 4-MeSC6H4, 175.4-7.2°; 5,6-(EtO)2, Ph, 123.0-5.2°; H, 2-pyridyl, -- (HCl salt m. 232.2-4.4°); 4-MeO, Ph, 177.2-82.2°; 5-MeO, Ph, 147.4-50.0°; 7-MeO, Ph, 122.0-5.2°; 6-Me, Ph, 174.2-5.2°; 6-EtO, Ph, 159.6-63.2°; 6-MeO, 2-ClC6H4, 125.2-8.8°; 6-MeO, 3-ClC6H4, 103.6-4.4°; 6-MeO, 3-MeOC6H4, 142.0-4.6°; 6-MeO, 2-EtOC6H4, 159.4-61.4°; 6-MeO, 2,6-Me2C6H3, 135.2-6.8°; 6-MeO, 2,5-MeOClC6H3, 121.8-8.6°; 5,6-(MeO)2, PhCH2 (XI), 113-14.4°; 5,6-EtO(MeO), Ph, 129.2-30.6°; 5,6-(MeO)2, 2-pyridyl -- (HCl salt m. 210.2-11.8°; 5,6-(OCH2CH2O), Ph, 170.8-6.8°; 5,6-(MeO)2, 2-EtOC6H4, 120.4-2.0°; 5,6-(MeO)2, 2,6-Me2C6H3, 117.8-19.6°; 5,6-(CH2O2), 4-MeOC6H4, 182.4-4.6°; 5,6-(CH2O2), 2-BuOC6H4, 125.0-6.4°; 5,6-(EtO)2, 2-MeOC6H4, 89.4-92.0°; 5,6-(EtO)2, 3-MeOC6H4, 97.6-8.4°; 6-Cl, Ph, 177.2-8.6°; 6-MeO, 2-pyridyl, 107.2-8.2°; 5,6-(MeO)2, 2-BuOC6H4, 93.8-5.8°; 5,6-(MeO)2, 2-EtC6H4, 104.2-7.2°; 5,6-(MeO)2, 2,5-(MeO)2C6H3, 136.8-7.8°; 5,6-(CH2O2), 2-pyridyl, -- (di-HCl salt m. 200-24°); 5,6-(MeO)2, 2-MeSC6H4, 116-17.8°. Also made were these I (n = 2; R1, R2, R3, R4, and m.p. given): H, Ph, Me, H, 154.2-5.6°; 5,6-(MeO)2, Ph, Me, H, -- (HCl salt m. 249.0-55.4°); 5,6-(CH2O2), 4-MeOC6H4, Me, H, 160.8-2.8°; 6-MeO, Ph, Me, H, -- (HCl salt m. 253.2-6.2°); 6-MeO, Ph, Ph, H, 148.2-8.8°; 5,6-(MeO)2, 2-MeOC6H4, Me, H, -- (di-HCl salt m. 217.4-20.8°); 5,6-(MeO)2, o-tolyl, Me, H, 119.8°-21.6°; 5,6-(MeO)2, m-tolyl, Me, H, -- (di-HCl salt m. 210.2-3.8°); 5,6-(MeO)2, 3-MeOC6H4, Me, H, -- (di-HCl salt m. 182.6-4.2°); 5,6-(CH2O2), 2-MeOC6H4, Me, H, 137.0-43.0°; 5,6-(CH2O2), 2-MeOC6H4, H, Me, 155.4-6.4°; 5,6-(MeO)2, Ph, Me, H, 139.6-40.4°; 5,6-(MeO)2, Ph, Et, H, --(HCl salt m. 237.6-9.0°); 5,6-(EtO)2, Ph, Me, H, 111.6-13.2°; 5,6-(CH2O2), 2-MeOC6H4, Me, Me, 118.2-19.6°; 5,6-(CH2O2), 2-MeOC6H4, Me, PhCH2, 169.2-70.2°; H, 2-MeOC6H4, H, Me, 74.6-6.4°.

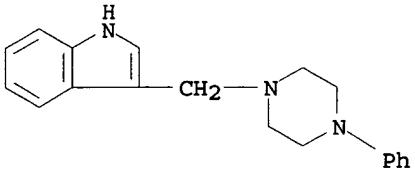
Catalytic debenzylation of XI gave I (R1 = 5,6-(MeO)2, R2, R3, R4 = H, n = 2), m. 109.6-11.4°, which reacted with 2-chloropyrimidine to give I (R1 = 5,6-(MeO)2, R2 = 2-pyrimidinyl, R3, R4 = H, n = 2), m. 127.2-8.2°. III (R4 = alkyl was reduced to II; other II were obtained as by-products in the LiAlH4 reduction of III. Thus were made these II (n = 1; R1, R2, R3, R4, and m.p. given): 5,6-(CH2O2), Ph, H, Me, 171-2.5°; 5,6-(MeO)2, Ph, H, Me, 128.4-30.2°; H, Ph, Me, Me, 136.8-9.6°; 5,6-(MeO)2, p-tolyl, H, H, 193.2-8.0°. Method C: On addition of 3-(4-benzhydryl-1-piperazinyl)propionyl chloride to a solution of 5-chloroindole and EtMgBr in ether, there was obtained IV (R1 = 5-Cl, R2 = Ph2CH, R3, R4 = H, n = 2) (XII), which with MeI and NaNH2 in liquid NH3 gave IV (R1 = 5-Cl, R2 = Ph2CH, R3 = H, R4 = Me, n = 2). Similarly made were these IV (R1, R2, R3,R4, and n given): H, Ph, Ph, H, 3; H, Ph, Ph, PhCH2, 3. XII was reduced by LiAlH4 to I (R1 = 5-Cl, R2 = Ph2CH, R3, R4 = H, n = 3), but XII reduced by **NaBH4** yielded II (R1 = 5-Cl, R2= Ph2CH, R3 = R4 = H, n = 2). When IV (R4 = alkyl) was reduced by LiAlH4, then II was obtained. Thus were made these II (R1, R2, R3, R4 and n given): 5-Cl, Ph2CH, H, Me, 2; H, Ph, Ph, PhCH2, 3; 6-BuO, Me, H, 4-MeSC6H4CH2CH2, 3; 5,6,7-(MeO)3, Me, H, 4-BuOC6H4CH2CH2, 3; H, Me, H, 3-HOC6H4CH2CH2, 3; H, Me, H, PhCH:CHCH2, 3. Method D: To a cold solution of 22.5 g. 3-indoleacetic acid and 13.3 g. Et3N in 800 ml. Me2CO was added 18.1 g. ClCO2Bu-iso, the mixture stirred for 10 min. at -10°, a solution of 1-phenylpiperazine in little Me2CO added, and the mixture kept 1.7 hrs. at room temperature to yield 5.4 g. V(R1, R2 = H, R3 = Ph, n = 1), m. 179.4-81.6°. Similarly

prepared were these V (R3 = H; R1, R2, n, and m.p. given): H, Ph, 2, 136.2-7.4°; H, 3-MeOC6H4, 1, --; H, 2-ClC6H4, 2, --; H, o-tolyl, 2, --; H, 2-MeOC6H4, 2, 173.0-6.0°; H, Ph, 3, --; H, 2-MeOC6H4, 3, 129-32°; H, 3-MeOC6H4, 3, --; 6-MeO, Ph, 2, 169-72°; 6-MeO, 2-MeOC6H4, 2, 120.5-2.0°; 5,6-(MeO)2, 3-ClC6H4, 1, --; 5,6-(CH2O2), Ph, 2, 178-80°; 5,6-(MeO)2, 2-ClC6H4, 1, 185-8.5°; 5,6-(MeO)2, 2-MeOC6H4, 2, 124.8-7.4°; 5,6-(MeO)2, Ph, 2, 120.5-2.0°; 5,6-(MeO)2, 3-MeOC6H4, 2, --. Also obtained was V [R1 = 5,6-(MeO)2, R2 = Ph, R3 = Me, n = 2). Also made was 1-[3-(1-indolyl)propionyl]-4-phenylpiperazine, an oil and 1-[3-(2-methyl-5,6-dimethoxy-3-indolyl)propionyl]-4-phenylpiperazine. By reduction of these V by LiAlH4 in VIII were prepared these I (R3 = R4 = H; R1, R2, n, and m.p. given): H, Ph, 2, --; H, Ph, 3, 126.6-7.8°; H, 3-MeOC6H4, 2, 146.4-7.6°; H, 2-ClC6H4, 3, 140.3-3.6°; H, o-tolyl, 3, 102.4-4.2°; H, 2-MeOC6H4, 3, 156.8-9.2°; H, Ph, 4, 96.0-100.8°; H, 2-MeOC6H4, 4, 120.6-3.8°; H, 3-MeOC6H4, 4, -- (HCl salt, m. 234.2-5.8°): 6-MeO, Ph, 3, 196.4-7.6°; 6-MeO, 2-MeOC6H4, 3, 153.2-5.0°; 5,6-di-MeO, 3-ClC6H4, 2, --(HCl salt m. 236.8-9.2°): 5,6-(CH2O2), Ph, 3, 142.6-4.2°; 5,6-(MeO)2, 2-ClC6H4, 2, 86.8-9.8°; 5,6-(MeO)2, 2-MeOC6H4, 3, 120.4-1.4°; 5,6-(MeO)2, Ph, 3, 157.4-8.2°; 5,6-(MeO)2, 3-MeOC6H4, 3, 159.0-60.2°. Also made was I (R1 = 5,6-(MeO)2, R2= Ph, R3 = Me, R4 = H, n = 3), m. 117.8-18.8°, and 1-[3-(1-indolyl)propyl]-4-phenylpiperazine, m. 96.7-8.4°. Method E: A solution of 9.0 g. indole in 100 ml. dioxane was added to a cold solution of 6.25 ml. 40% aqueous CH2O and 13.3 g. 1-phenylpiperazine in 1 l. dioxane to give I (R1 = R3 = R4 = H, R2 = Ph, n = 1), m. 184.6-6.8°. Similarly made was I (R1 = 5,6-(MeO)2, R2 = Ph, R3 = R4 = H, n = 1), m. 159.3-60.2°. Method F: The piperazine ring was formed after a substituted ethylenediamine group had been joined to the indole moiety. Thus, 27 g. IX and 58 g. (PhCH2)NPhCH2CH2NH2 in 300 ml. VIII refluxed for 5 hrs. gave 41.9 g. N-benzyl-N-phenyl-N'-[(3-indolyl)glyoxalyl]ethylenediamine, m. 162.2-2.8°, which was reduced by LiAlH4 to N-benzyl-N-phenyl-N'-[2-(3-indolyl)ethyl]ethylenediamine (XIII) (di-HCl salt m. 171.4-5.4°). Also made were N-benzyl-N-methyl-N'-[(3-indolyl)glyoxalyl]ethylenediamine, m. 124.5-7.0°, and N-benzyl-N-methyl-N'-[2-(3-indolyl)ethyl]ethylenediamine, m. 102-5°. A solution of 11.1 g. XIII and 3.4 g. ClCH2COCl in CH2Cl2 was refluxed to yield 9.4 g. 4-[2-(3-indolyl)ethyl]-1-phenyl-1-benzyl-1m3-oxopiperazinium chloride, m. 157-9.5°, which was **catalytically** debenzylated to 1-[2-(3-indolyl)ethyl]-4-phenyl-2-piperazinone, m. 157.2-9.0°. Similarly made was 4-[2-(3-indolyl)ethyl]-1-methyl-1-benzyl-3-oxopiperazinium chloride, m. 229.5-32.5°, and 4-[2-(3-indolyl)ethyl]-2-methyl-1-phenyl-3-piperazinone, m. 186.4-91.8°. The latter, reduced by LiAlH4, gave 1-[2-(3-indolyl)ethyl]-3-methyl-4-phenylpiperazine, m. 116.2-17.6°.

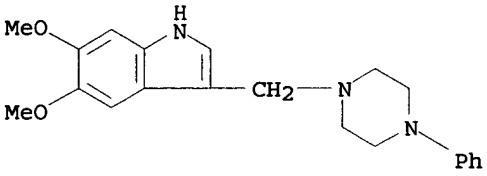
IT **4281-72-5**, Indole, 3-[(4-phenyl-1-piperazinyl)methyl]-
4281-76-9, Indole, 5,6-dimethoxy-3-[(4-phenyl-1-piperazinyl)methyl]-
(preparation of)

RN 4281-72-5 HCAPLUS

CN 1H-Indole, 3-[(4-phenyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 4281-76-9 HCAPLUS
CN 1H-Indole, 5,6-dimethoxy-3-[(4-phenyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



IC C07C; C07D
CC 38 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 153-87-7, Indole, 5,6-dimethoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 1866-99-5, Indole, 5,6-dimethoxy-2-methyl-3-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, dihydrochloride 4121-77-1, Indole, 2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4281-70-3, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-6-methyl- 4281-71-4, Indole, 5,6-dimethoxy-3-[2-[4-(m-methoxyphenyl)-1-piperazinyl]ethyl]-2-methyl-, dihydrochloride **4281-72-5**, Indole, 3-[(4-phenyl-1-piperazinyl)methyl]- 4281-73-6, Indole, 3-[3-(4-phenyl-1-piperazinyl)propyl]- 4281-74-7, Indole, 3-[4-(4-phenyl-1-piperazinyl)butyl]- 4281-75-8, Indole, 6-methoxy-3-[3-(4-phenyl-1-piperazinyl)propyl]- **4281-76-9**, Indole, 5,6-dimethoxy-3-[(4-phenyl-1-piperazinyl)methyl]- 4281-77-0, 5H-1,3-Dioxolo[4,5-f]indole, 7-[3-(4-phenyl-1-piperazinyl)propyl]- 4281-78-1, Indole, 3-[3-[4-(o-methoxyphenyl)-1-piperazinyl]propyl]- 4281-79-2, Indole, 3-[4-[4-(o-methoxyphenyl)-1-piperazinyl]butyl]- 4281-80-5, Indole, 6-methoxy-3-[3-[4-(o-methoxyphenyl)-1-piperazinyl]propyl]- 4281-81-6, Indole, 5,6-dimethoxy-3-[3-[4-(o-methoxyphenyl)-1-piperazinyl]propyl]- 4281-82-7, Indole, 3-[2-[4-(o-ethylphenyl)-1-piperazinyl]-ethyl]-5,6-dimethoxy- 4281-83-8, Indole, 5,6-dimethoxy-3-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-2-methyl-, dihydrochloride 4293-81-6, Indole, 6-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4293-82-7, Indole, 5-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4293-83-8, Indole, 5,6-dimethoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4293-84-9, Indole, 6-ethoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4293-85-0, Indole, 5,6-diethoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4293-86-1, Indole, 5-ethoxy-6-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4293-87-2, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-(4-phenyl-1-piperazinyl)ethyl]- 4293-88-3, Indole, 3-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]- 4293-89-4, Indole, 6-methoxy-3-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]- 4293-90-7, Indole, 5,6-dimethoxy-3-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]- 4342-15-8, Indole, 5,6-dimethoxy-3-[2-(1-piperazinyl)ethyl]- 4342-16-9, Indole, 3-[2-(4-benzyl-1-piperazinyl)ethyl]-5,6-dimethoxy- 4366-55-6, Indole, 3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4417-95-2, Indole, 6-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 4448-96-8, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(o-methoxyphenyl)-1-

piperazinyl]ethyl]- 4448-97-9, Indole, 3-[2-[4-(m-methoxyphenyl)-1-piperazinyl]ethyl]- 4448-98-0, Indole, 6-methoxy-3-[2-[4-(m-methoxyphenyl)-1-piperazinyl]ethyl]- 4448-99-1, Indole, 5,6-diethoxy-3-[2-[4-(m-methoxyphenyl)piperazinyl]ethyl]- 4449-00-7, Indole, 3-[2-[4-(p-methoxyphenyl)-1-piperazinyl]ethyl]- 4449-01-8, Indole, 5,6-dimethoxy-3-[2-[4-(p-methoxyphenyl)-1-piperazinyl]ethyl]- 4449-02-9, Indole, 3-[2-[4-(o-ethoxyphenyl)-1-piperazinyl]ethyl]-6-methoxy- 4449-03-0, Indole, 3-[2-(4-o-tolyl-1-piperazinyl)ethyl]- 4449-04-1, Indole, 6-methoxy-3-[2-(4-o-tolyl-1-piperazinyl)ethyl]- 4449-06-3, Indole, 6-methoxy-3-[2-(4-m-tolyl-1-piperazinyl)ethyl]- 4449-07-4, Indole, 5,6-dimethoxy-3-[2-(4-m-tolyl-1-piperazinyl)ethyl]- 4449-08-5, Indole, 3-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 4449-09-6, Indole, 6-methoxy-3-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 4449-10-9, Indole, 5,6-dimethoxy-3-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 4449-11-0, Indole, 3-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy- 4449-12-1, Indole, 3-[2-[4-(m-chlorophenyl)-1-piperazinyl]ethyl]-6-methoxy- 4449-16-5, Indole, 5,6-dimethoxy-3-[3-(4-phenyl-1-piperazinyl)propyl]- 4449-17-6, Indole, 5,6-dimethoxy-2-methyl-3-[3-(4-phenyl-1-piperazinyl)propyl]- 4533-22-6, Indole, 5,6-dimethoxy-2-methyl-3-[2-(4-o-tolyl-1-piperazinyl)ethyl]- 4554-08-9, Indole, 6-methoxy-3-[2-[4-(2-pyridyl)-1-piperazinyl]ethyl]- 4558-73-0, Indole, 3-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]-6-methoxy- 4644-97-7, Indole, 3-[2-(1-piperazinyl)ethyl]- 5174-05-0, Indole, 6-methoxy-3-[2-[4-(p-methoxyphenyl)-1-piperazinyl]ethyl]- 5174-06-1, Indole, 3-[2-[4-(o-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy- 5174-07-2, Indole, 3-[2-(4-m-tolyl-1-piperazinyl)ethyl]- 5567-55-5, Indole, 5,6-diethoxy-3-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]- 5567-56-6, Indole, 5,6-dimethoxy-3-[2-[4-(m-methoxyphenyl)-1-piperazinyl]ethyl]- 6560-23-2, Piperazine, 1-benzyl-4-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]- 17506-57-9, Indole, 3-[2-[4-(p-chlorophenyl)-1-piperazinyl]ethyl]- 17506-59-1, Indole, 3-[2-(4-methyl-1-piperazinyl)ethyl]-, dihydrochloride 17506-60-4, 1-Piperazineethanol, 4-(2-indol-3-ylethyl)-, dihydrochloride 17506-63-7, Indole, 5-(benzyloxy)-3-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 17506-68-2, Indole, 6-methoxy-2-phenyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 17506-69-3, Indole, 6-chloro-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 17506-70-6, 5H-1,3-Dioxolo[4,5-f]indole, 5-benzyl-7-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-6-methyl- 17506-71-7, Indole, 1-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 25674-12-8, Indol-5-ol, 3-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 25674-13-9, Indole, 5-methoxy-3-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 25680-48-2, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-5,6-dimethyl- 25680-49-3, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-5-methyl- 25680-50-6, Indole, 3-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-1-methyl- 25699-32-5, Indole, 5,6-dimethoxy-3-[2-[4-(2,6-xylyl)-1-piperazinyl]ethyl]- 25699-34-7, Indole, 6-methoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride 25699-36-9, 6H-p-Dioxino[2,3-f]indole, 2,3-dihydro-8-[2-(4-phenyl-1-piperazinyl)ethyl- 25699-37-0, Indole, 3-[3-(4-o-tolyl-1-piperazinyl)propyl]- 25699-39-2, Indole, 3-[3-[4-(o-chlorophenyl)-1-piperazinyl]propyl]- 25699-48-3, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(o-butoxyphenyl)-1-piperazinyl]ethyl]- 25699-50-7, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(2-pyridyl)-1-piperazinyl]ethyl]-, dihydrochloride 25699-55-2, Indole, 3-[2-[4-(o-butoxyphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy- 25699-58-5, Indole, 3-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy- 25699-59-6, Indole, 5,6-dimethoxy-3-[2-[4-(2-pyrimidinyl)-1-piperazinyl]ethyl]- 25699-61-0, Indole, 5,6-diethoxy-2-methyl-3-[2-(4-phenyl-1-

piperazinyl)ethyl]- 25699-62-1, Indole, 5,6-dimethoxy-3-[2-[4-[o-(methylthio)phenyl]-1-piperazinyl]ethyl]- 25699-64-3, Indole, 5,6-dimethoxy-3-[3-[4-(m-methoxyphenyl)-1-piperazinyl]propyl]- 25701-56-8, Indole, 5-(methylthio)-3-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 25701-57-9, Indol-5-ol, 3-[2-(4-phenethyl-1-piperazinyl)ethyl]- 25701-59-1, Indole, 5-(methylthio)-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 25701-60-4, Indole, 3-[2-[4-(3-chloro-p-tolyl)-1-piperazinyl]ethyl]- 25701-65-9, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-(4-p-tolyl-1-piperazinyl)ethyl]- 25701-74-0, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-(4-m-tolyl-1-piperazinyl)ethyl]- 25701-77-3, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-(4-o-tolyl-1-piperazinyl)ethyl]- 25701-79-5, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(p-methoxyphenyl)-1-piperazinyl]ethyl]-6-methyl- 25701-84-2, Indole, 5,6-dimethoxy-3-[2-[4-[p-(methylthio)phenyl]-1-piperazinyl]ethyl]- 25701-88-6, 5H-1,3-Dioxolo[4,5-f]indole, 7-[2-[4-(p-methoxyphenyl)-1-piperazinyl]ethyl]- 25701-97-7, Indole, 3-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-6-methoxy- 25701-98-8, Indole, 6-methoxy-3-[2-[4-(2,6-xylyl)-1-piperazinyl]ethyl]- 25701-99-9, Indole, 4-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 25774-94-1, Indole, 7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- 40523-01-1, Indole, 5,6-dimethoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride 42204-19-3, Indole, 2-ethyl-5,6-dimethoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, hydrochloride 71765-56-5, Piperazine, 1-(indol-3-ylglyoxyloyl)-4-phenyl- 75889-28-0, 2-Piperazinone, 1-(2,6-xylyl)-, hydrochloride 81807-97-8, Piperazine, 1-(indol-3-ylacetyl)-4-phenyl- 88048-40-2, Piperazine, 1-(5H-1,3-dioxolo[4,5-f]indol-7-ylglyoxyloyl)-4-phenyl- 88616-96-0, Piperazine, 1-[(6-chloroindol-3-yl)glyoxyloyl]-4-phenyl- 90917-86-5, 2-Piperazinone, 1-phenyl- 93149-47-4, Indole, 3-[2-(2,5-dimethyl-1-piperazinyl)ethyl]- 94254-78-1, Piperazine, 1-(indol-3-ylglyoxyloyl)-4-(2-pyridyl)- 94579-62-1, Piperazine, 1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-(2-pyridyl)- 94685-76-4, 2-Piperazinone, 1-(2-indol-3-ylethyl)-4-phenyl- 94685-77-5, 2-Piperazinone, 4-(2-indol-3-ylethyl)-1-phenyl- 94862-78-9, Piperazine, 1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-(2-pyridyl)- 94912-85-3, Indole, 3-[2-[[2-(benzylmethylamino)ethyl]amino]ethyl]- 94918-70-4, Piperazine, 1-(3-indol-1-ylpropionyl)-4-phenyl- 94918-71-5, Piperazine, 1-(3-indol-3-ylpropionyl)-4-phenyl- 94918-72-6, 2-Piperazinone, 1-(2-indol-3-ylethyl)-3-methyl-4-phenyl- 94961-31-6, Indole, 3-[2-(3-methyl-4-phenyl-1-piperazinyl)ethyl]- 94961-32-7, Indole, 1-[3-(4-phenyl-1-piperazinyl)propyl]- 95002-94-1, Piperazine, 1-(3-chloro-p-tolyl)-4-(indol-3-ylglyoxyloyl)- 95002-96-3, Piperazine, 1-(o-chlorophenyl)-4-[(6-methoxyindol-3-yl)glyoxyloyl]- 95131-10-5, Piperazine, 1-[[5-(methylthio)indol-3-yl]glyoxyloyl]-4-p-tolyl- 95131-14-9, Piperazine, 1-[(6-ethoxyindol-3-yl)glyoxyloyl]-4-phenyl- 95131-15-0, Piperazine, 1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-o-tolyl- 95131-16-1, Piperazine, 1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-p-tolyl- 95131-17-2, Piperazine, 1-[(6-methoxy-2-methylindol-3-yl)glyoxyloyl]-4-phenyl- 95131-20-7, Piperazine, 1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-phenyl- 95131-21-8, Piperazine, 1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-(o-methoxyphenyl)- 95131-22-9, Piperazine, 1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-(p-methoxyphenyl)- 95138-73-1, Methanesulfonic acid, compound with 3-[2-(4-p-tolyl-1-piperazinyl)ethyl] indol-5-ol 95226-89-4, Piperazine, 1-(3-indol-3-ylpropionyl)-4-(o-methoxyphenyl)- 95226-90-7, Piperazine, 1-[3-(6-methoxyindol-3-yl)propionyl]-4-phenyl- 95291-47-7, Piperazine, 1-(o-chlorophenyl)-4-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]- 95439-11-5, Indole, 3-[2-(4-cinnamyl-1-piperazinyl)ethyl]- 95439-25-1, Piperazine, 1-(4-indol-3-ylbutyryl)-4-(o-methoxyphenyl)- 95439-31-9, Piperazine, 1-[3-(5,6-dimethoxyindol-3-yl)propionyl]-4-phenyl- 95439-32-0, Piperazine,

1-[3-(6-methoxyindol-3-yl)propionyl]-4-(o-methoxyphenyl)-
95440-09-8, Indole-3-methanol, 5,6-dimethoxy-α-[(4-p-tolyl-1-
piperazinyl)methyl]- 95441-94-4, Piperazine,
1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-(2,6-xylyl)- 95441-96-6,
Piperazine, 1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-o-tolyl-
95441-97-7, Piperazine, 1-[(5,6-dimethoxy-2-methylindol-3-
yl)glyoxyloyl]-4-phenyl- 95441-98-8, Piperazine,
1-[(5-ethoxy-6-methoxyindol-3-yl)glyoxyloyl]-4-phenyl-
95441-99-9, Piperazine, 1-(o-ethoxyphenyl)-4-[(6-methoxyindol-3-
yl)glyoxyloyl]- 95442-00-5, Piperazine, 1-[(5,6-dimethoxyindol-3-
yl)glyoxyloyl]-4-[o-(methylthio)phenyl]- 95442-02-7, Piperazine,
1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-(o-methoxyphenyl)-
95442-03-8, Piperazine, 1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-
(p-methoxyphenyl)- 95698-78-5, Piperazine, 1-[3-(5,6-
dimethoxyindol-3-yl)propionyl]-4-(o-methoxyphenyl)- 95821-61-7,
Piperazine, 1-[(5,6-diethoxyindol-3-yl)glyoxyloyl]-4-(o-
methoxyphenyl)- 95822-99-4, Indole-3-glyoxylamide,
N-[2-(N-benzylanilino)ethyl]- 95940-38-8, Piperazine,
1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-(m-methoxyphenyl)-
95957-02-1, Piperazine, 1-[(5,6-diethoxyindol-3-yl)glyoxyloyl]-4-
phenyl- 95957-03-2, Piperazine, 1-[(5,6-dimethoxyindol-3-
yl)glyoxyloyl]-4-(o-ethylphenyl)- 95957-04-3, Piperazine,
1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-(2,6-xylyl)-
95957-05-4, Piperazine, 1-[(5,6-dimethoxy-2-methylindol-3-
yl)glyoxyloyl]-4-o-tolyl- 95957-06-5, Piperazine,
1-[(2-ethyl-5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-phenyl-
95957-08-7, Piperazine, 1-[(5,6-dimethoxy-2-methylindol-3-
yl)glyoxyloyl]-4-(o-methoxyphenyl)- 96072-50-3, Piperazine,
1-(o-butoxyphenyl)-4-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-
96178-08-4, Piperazine, 1-[(6-methoxy-2-phenylindol-3-
yl)glyoxyloyl]-4-phenyl- 96216-58-9, Piperazine,
1-[[5-(benzyloxy)indol-3-yl]glyoxyloyl]-4-p-tolyl- 96216-73-8,
1-Propanone, 1-(5-chloroindol-3-yl)-3-[4-(diphenylmethyl)-1-
piperazinyl]- 96264-25-4, Indole, 5-chloro-3-[3-[4-
(diphenylmethyl)-1-piperazinyl]propyl]- 96264-26-5,
Indole-3-methanol, 5-chloro-α-[2-[4-(diphenylmethyl)-1-
piperazinyl]ethyl]- 96265-41-7, Piperazine, 1-benzyl-4-(indol-3-
ylglyoxyloyl)- 96265-42-8, Piperazine, 1-(indol-3-ylglyoxyloyl)-
4-o-tolyl- 96265-45-1, Piperazine, 1-(indol-3-ylglyoxyloyl)-4-(p-
methoxyphenyl)- 96265-46-2, Piperazine, 1-[(5-methoxyindol-3-
yl)glyoxyloyl]-4-phenyl- 96265-47-3, Piperazine,
1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-phenyl- 96265-80-4,
Piperazine, 1-(m-chlorophenyl)-4-[(6-methoxyindol-3-yl)glyoxyloyl]-
96266-49-8, Piperazine, 1-(o-chlorophenyl)-4-[(5,6-
dimethoxyindol-3-yl)acetyl]- 96310-69-9, Indole,
5-(benzyloxy)-3-[2-(4-phenethyl-1-piperazinyl)ethyl]-
96365-50-3, Indole-3-methanol, 5,6-dimethoxy-1-methyl-α-[(4-
phenyl-1-piperazinyl)methyl]- 96370-68-2, Piperazine,
1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-m-tolyl- 96370-70-6,
Piperazine, 1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-[p-
(methylthio)phenyl]- 96370-72-8, Piperazine,
1-[(5,6-dimethoxyindol-3-yl)glyoxyloyl]-4-(m-methoxyphenyl)-
96372-19-9, Piperazine, 1-[[5-(benzyloxy)indol-3-yl]glyoxyloyl]-4-
phenethyl- 96372-30-4, 1-Propanone, 1-(5-chloro-1-methylindol-3-
yl)-3-[4-(diphenylmethyl)-1-piperazinyl]- 96578-13-1,
Piperazine, 1-(5-chloro-2-methoxyphenyl)-4-[(6-methoxyindol-3-
yl)glyoxyloyl]- 96669-66-8, Piperazine, 1-[(5,6-dimethoxyindol-3-
yl)glyoxyloyl]-4-(o-ethoxyphenyl)- 96669-67-9, Piperazine,
1-[(5,6-dimethoxy-2-methylindol-3-yl)glyoxyloyl]-4-(m-
methoxyphenyl)- 96669-69-1, Piperazine, 1-[(5,6-dimethoxyindol-3-
yl)glyoxyloyl]-4-(2,5-dimethoxyphenyl)- 96711-96-5, 1-Butanone,
1-(1-benzyl-2-phenylindol-3-yl)-4-(4-phenyl-1-piperazinyl)-
97074-57-2, Indole, 3-[2-[[2-(N-benzylanilino)ethyl]amino]ethyl]-,
dihydrochloride 97153-24-7, Piperazine, 1-[(5,6-diethoxy-2-
methylindol-3-yl)glyoxyloyl]-4-phenyl- 97153-26-9, Piperazine,
1-[(5,6-diethoxyindol-3-yl)glyoxyloyl]-4-(m-methoxyphenyl)-

98107-12-1, Indole-3-glyoxylamide, N-[2-(benzylmethylamino)ethyl]-
98657-76-2, 2-Piperazinone, 1-phenyl-, p-toluenesulfonate
98843-67-5, Piperazine, 1-(5H-1,3-dioxolo[4,5-f]indol-7-
ylglyoxyloyl)-4-(2-methoxyethyl)- 99000-15-4, Indole,
3-[2-[4-(2-pyridyl)-1-piperazinyl]ethyl]-, hydrochloride
100167-53-1, Piperazine, 1-(5H-1,3-dioxolo[4,5-f]indol-7-
ylglyoxyloyl)-4-(2-pyridyl)- 100211-33-4, 2-Piperazinone,
4-benzyl-1-(2,6-xylyl)-, hydrochloride 100233-69-0, Piperazine,
1-[(5-methyl-5H-1,3-dioxolo[4,5-f]indol-7-yl)glyoxyloyl]-4-phenyl-
100261-72-1, Piperazine, 1-[3-(5H-1,3-dioxolo[4,5-f]indol-7-
yl)propionyl]-4-phenyl- 100265-84-7, Piperazine,
1-[(2,3-dihydro-6H-p-dioxino[2,3-f]indol-8-yl)glyoxyloyl]-4-phenyl-
100265-85-8, Piperazine, 1-(5H-1,3-dioxolo[4,5-f]indol-7-
ylglyoxyloyl)-4-m-tolyl- 100265-86-9, Piperazine,
1-(5H-1,3-dioxolo[4,5-f]indol-7-ylglyoxyloyl)-4-(p-methoxyphenyl)-
100265-88-1, Piperazine, 1-(5H-1,3-dioxolo[4,5-f]indol-7-
ylglyoxyloyl)-4-o-tolyl- 100269-25-8, Piperazine,
1-[(6-methoxyindol-3-yl)glyoxyloyl]-4-m-tolyl- 100576-00-9,
1-Benzyl-4-(2-indol-3-ylethyl)-1-methyl-3-oxopiperazinium chloride
100731-59-7, Indole, 5,6-dimethoxy-3-[2-[4-(2-pyridyl)-1-
piperazinyl]ethyl]-, hydrochloride 100770-19-2,
5H-1,3-Dioxolo[4,5-f]indole-7-methanol, 5-methyl-α-[(4-
phenyl-1-piperazinyl)methyl]- 100916-04-9, Indole,
3-[2-[4-(m-chlorophenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-,
hydrochloride 101058-73-5, Indole, 5,6-dimethoxy-3-[2-(4-o-tolyl-
1-piperazinyl)ethyl]-, hydrochloride 101122-25-2, Piperazine,
1-(p-methoxyphenyl)-4-[(6-methyl-5H-1,3-dioxolo[4,5-f]indol-7-
yl)glyoxyloyl]- 101122-26-3, Piperazine, 1-(o-methoxyphenyl)-4-
[(6-methyl-5H-1,3-dioxolo[4,5-f]indol-7-yl)glyoxyloyl]-
101227-73-0, Indole, 3-[4-[4-(m-methoxyphenyl)-1-
piperazinyl]butyl]-, hydrochloride 101896-73-5, Piperazine,
1-[(5,6-dimethoxy-2-methylindol-3-yl)glyoxyloyl]-4-m-tolyl-
102263-61-6, 1-Benzyl-4-(2-indol-3-ylethyl)-3-oxo-1-
phenylpiperazinium chloride 103652-33-1, Piperazine,
1-(o-butoxyphenyl)-4-(5H-1,3-dioxolo[4,5-f]indol-7-ylglyoxyloyl)-
104780-99-6, Indole-3-methanol, 1,2-dimethyl-α-[(4-phenyl-1-
piperazinyl)methyl]- 104878-48-0, Acetanilide,
2,4'-dichloro-N-[2-(dibenzylamino)ethyl]-, hydrochloride
105146-98-3, Piperazine, 1-[[5-(methylthio)indol-3-yl]glyoxyloyl]-
4-phenyl- 360561-52-0, 2-Piperazinone, 1-(p-chlorophenyl)-,
hydrochloride 875833-82-2, Piperazine, 1-(5H-1,3-dioxolo[4,5-
f]indol-7-ylglyoxyloyl)-4-p-tolyl-
(preparation of)

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=> => d que stat l107
L41             SCR 1918 OR 2043
L42             SCR 1994
L43             SCR 1607
L44             STR
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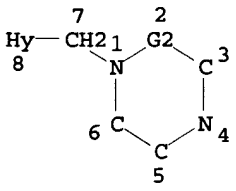


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REP G2=(0-1) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS UNS  AT   8
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1 C  M1 N  AT   8
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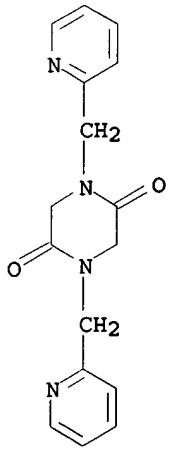
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE
L45 SCR 1842
L46 SCR 1996
L47 SCR 1608
L48 13366 SEA FILE=REGISTRY SSS FUL L44 AND L47 AND L42 AND L43 NOT (L41 OR L45 OR L46)
L92 51 SEA FILE=CAOLD ABB=ON PLU=ON L48
L106 QUE ABB=ON PLU=ON PRODUC? OR PROD# OR GENERAT? OR MANUF? OR MFR# OR CREAT? OR FORM## OR FORMING# OR FORMAT? OR MAKE# OR MADE# OR MAKIN# OR FABRICAT? OR SYNTHESI? OR PREPAR? OR PREP#
L107 8 SEA FILE=CAOLD ABB=ON PLU=ON L92 AND L106

=> => d l107 1-8 all hitstr

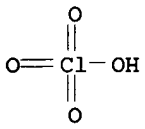
L107 ANSWER 1 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA65:5459c CAOLD
TI condensations of acylpyridines with amines - (I) 2-acylpyridines and aminoacetal
AU Glover, E. E.; Jones, G.; Trenholm, G.
TI **synthesis** of potential antineoplastic agents - (XIV) 2-substituted 2,3-dihydro-1H-perimidines
AU Wasulko, William; Noble, A. C.; Popp, F. D.
IT 645-36-3 5745-83-5 5745-91-5 5745-92-6 5983-01-7
6584-37-8 6584-38-9 6584-39-0 6584-40-3 6584-41-4
6584-42-5 6584-45-8 6584-47-0 6584-49-2 6584-51-6
6584-52-7 6584-54-9 **6584-55-0** **6584-56-1**
6584-57-2 **6584-58-3** **6592-01-4**
6592-02-5 6592-03-6 6592-04-7 6592-05-8 6592-06-9
6592-07-0 6592-08-1 6592-09-2 6592-10-5 6592-11-6
6662-96-0 6662-97-1 6663-33-8 6672-87-3 6697-86-5
6721-12-6 6721-13-7 6721-14-8 6723-15-5 6723-16-6
6747-38-2 6758-91-4 6758-92-5 **6868-47-9**
10516-79-7 97302-46-0 97832-20-7
IT **6584-55-0** **6584-56-1** **6584-57-2**
6584-58-3 **6592-01-4** **6868-47-9**
10516-79-7
RN 6584-55-0 CAOLD
CN 2,5-Piperazinedione, 1,4-bis(2-pyridylmethyl)- (7CI, 8CI) (CA INDEX NAME)



RN 6584-56-1 CAOLD
CN 2,5-Piperazinedione, 1,4-bis(2-pyridylmethyl)-, diperchlorate (8CI) (CA INDEX NAME)

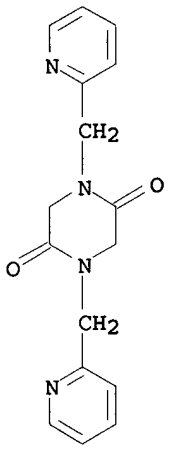
CM 1

CRN 7601-90-3
CMF Cl H O4



CM 2

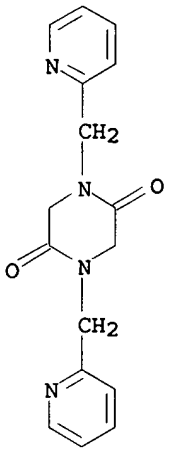
CRN 6584-55-0
CMF C16 H16 N4 O2



RN 6584-57-2 CAOLD
CN 2,5-Piperazinedione, 1,4-bis(2-pyridylmethyl)-, dipicrate (7CI, 8CI) (CA INDEX NAME)

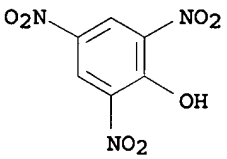
CM 1

CRN 6584-55-0
CMF C16 H16 N4 O2

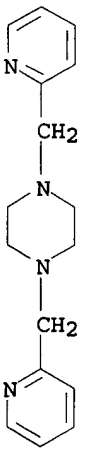


CM 2

CRN 88-89-1
CMF C6 H3 N3 O7



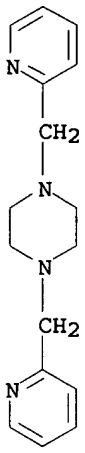
RN 6584-58-3 CAOLD
CN Piperazine, 1,4-bis(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



RN 6592-01-4 CAOLD
CN Piperazine, 1,4-bis(2-pyridylmethyl)-, dimethiodide (7CI, 8CI)
(CA INDEX NAME)

CM 1

CRN 6584-58-3
CMF C16 H20 N4



CM 2

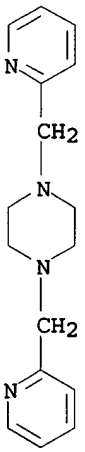
CRN 74-88-4
CMF C H3 I

H_3C-I

RN 6868-47-9 CAOLD
CN Piperazine, 1,4-bis(2-pyridylmethyl)-, tetrapicrate (7CI, 8CI)
(CA INDEX NAME)

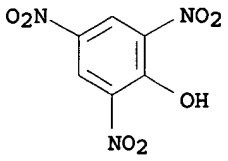
CM 1

CRN 6584-58-3
CMF C16 H20 N4

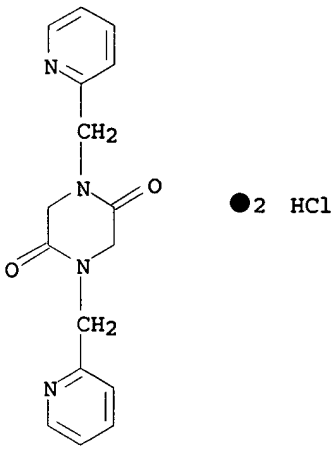


CM 2

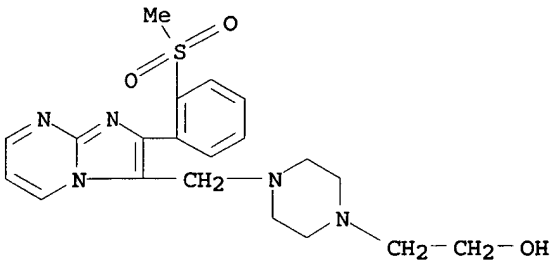
CRN 88-89-1
CMF C6 H3 N3 O7



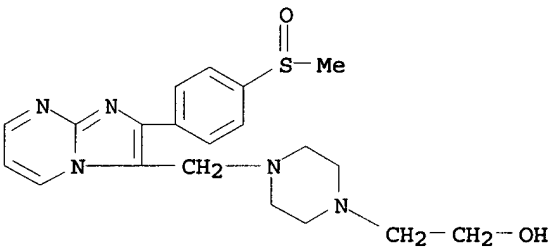
RN 10516-79-7 CAOLD
CN 2,5-Piperazinedione, 1,4-bis(2-pyridylmethyl)-, dihydrochloride (8CI) (CA INDEX NAME)



L107 ANSWER 2 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA64:5070g CAOLD
TI derivs. of imidazole - (II) **synthesis** and reactions of imidazo-[1,2-α]pyrimidines and other bi- and tricyclic imidazo derivs. with analgesic, antiinflammatory, antipyretic, and anticonvulsant activity
AU Almirante, Luigi; Polo Friz, L.; Mugnaini, A.; Provinciali, E.; Rugarli, P.; Gamba, A.; Olivi, A.; Murmann, W.
IT 3415-13-2 3415-15-4 3415-16-5 3415-18-7 3415-19-8
3415-20-1 3415-21-2 3415-22-3 3458-53-5 3458-54-6
3458-55-7 3458-56-8 **3458-58-0** **3458-61-5**
3458-62-6 **3458-63-7** 3851-21-6 7001-75-4
94521-13-8 95980-00-0
IT **3458-58-0** **3458-61-5** **3458-63-7**
RN 3458-58-0 CAOLD
CN 1-Piperazineethanol, 4-[[2-[2-(methylsulfonyl)phenyl]imidazo[1,2-a]pyrimidin-3-yl]methyl]- (9CI) (CA INDEX NAME)

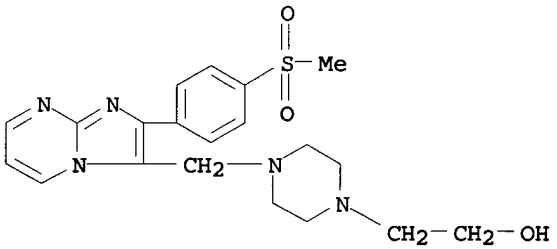


RN 3458-61-5 CAOLD
CN 1-Piperazineethanol, 4-[[2-[4-(methylsulfinyl)phenyl]imidazo[1,2-a]pyrimidin-3-yl]methyl]-, trihydrochloride (9CI) (CA INDEX NAME)

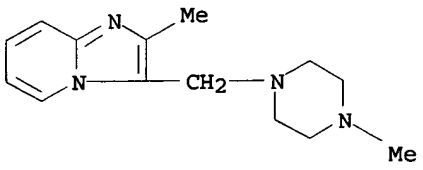


●3 HCl

RN 3458-63-7 CAOLD
CN 1-Piperazineethanol, 4-[[2-[4-(methylsulfonyl)phenyl]imidazo[1,2-a]pyrimidin-3-yl]methyl]- (9CI) (CA INDEX NAME)

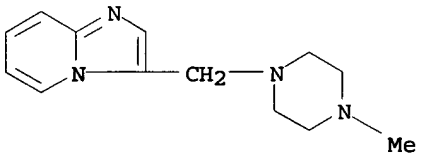


L107 ANSWER 3 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA63:5629h CAOLD
TI **preparation** and reactions of imidazo[1,2-a]pyridines
AU Lombardino, Joseph G.
IT 274-76-0 2549-17-9 2549-18-0 2549-19-1 2549-20-4
2549-26-0 2549-28-2 2717-91-1 2717-92-2 2717-93-3
2717-94-4 2717-95-5 2717-96-6 2717-97-7 2717-98-8
2717-99-9 **2718-00-5** 2718-01-6 2718-02-7
3100-90-1 4098-14-0 6798-99-8
IT **2718-00-5** **3100-90-1**
RN 2718-00-5 CAOLD
CN Imidazo[1,2-a]pyridine, 2-methyl-3-[(4-methyl-1-piperazinyl)methyl]-, trihydrochloride (7CI, 9CI) (CA INDEX NAME)



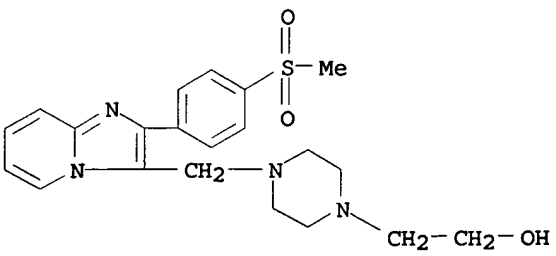
●3 HCl

RN 3100-90-1 CAOLD
CN Imidazo[1,2-a]pyridine, 3-[(4-methyl-1-piperazinyl)methyl]-, trihydrochloride (7CI, 8CI) (CA INDEX NAME)

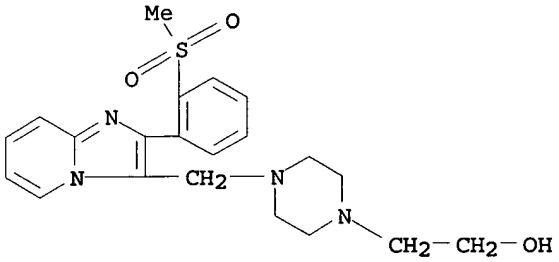


●3 HCl

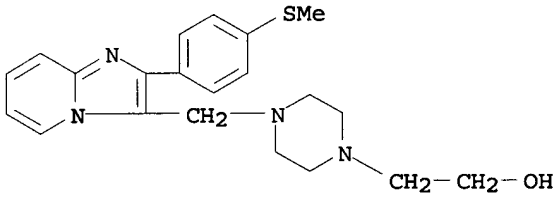
L107 ANSWER 4 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA62:16228a CAOLD
TI derivs. of imidazole - (I) **synthesis** and reactions of imidazo [1,2-a] pyridines with analgesic, antiinflammatory, antipyretic, and anticonvulsant activity
AU Almirante, Luigi; Polo Friz, L.; Mugnaini, A.; Provinciali, E.; Rugarli, P.; Biancotti, A.; Gamba, A.; Murmann, W.
IT 1155-08-4 2076-70-2 2076-74-6 **2609-67-8**
3173-95-3 3268-57-3 3323-01-1 3323-02-2 3323-03-3
3323-08-8 3323-09-9 3323-10-2 3323-11-3 3323-12-4
3323-13-5 3323-14-6 3323-15-7 3323-16-8 3323-17-9
3323-18-0 3323-20-4 3323-21-5 **3323-22-6**
3323-24-8 **3323-25-9** 3323-26-0 3323-66-8
3323-68-0 3323-69-1 3323-70-4 3369-04-8 3369-09-3
3369-10-6 3369-13-9 3441-47-2 3504-04-9 **3520-03-4**
3672-37-5 3999-29-9 105042-63-5
IT **2609-67-8** **3323-22-6** **3323-25-9**
3520-03-4
RN 2609-67-8 CAOLD
CN 1-Piperazineethanol, 4-[[2-[p-(methylsulfonyl)phenyl]imidazo[1,2-a]pyridin-3-yl]methyl]- (7CI, 8CI) (CA INDEX NAME)



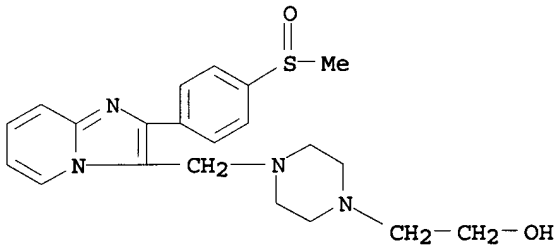
RN 3323-22-6 CAOLD
CN 1-Piperazineethanol, 4-[[2-[o-(methylsulfonyl)phenyl]imidazo[1,2-a]pyridin-3-yl]methyl]- (7CI, 8CI) (CA INDEX NAME)



RN 3323-25-9 CAOLD
CN 1-Piperazineethanol, 4-[[2-[p-(methylthio)phenyl]imidazo[1,2-a]pyridin-3-yl]methyl]- (7CI, 8CI) (CA INDEX NAME)



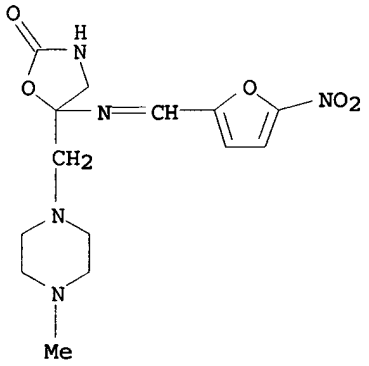
RN 3520-03-4 CAOLD
CN 1-Piperazineethanol, 4-[[2-[p-(methylsulfinyl)phenyl]imidazo[1,2-a]pyridin-3-yl]methyl]-, trihydrochloride (7CI, 8CI) (CA INDEX NAME)



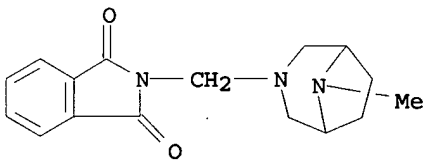
●3 HCl

L107 ANSWER 5 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA60:15851d CAOLD
TI **preparation** and pharmacol. properties of some N-(5-nitro-2-furfurylidene)-3-aminomethyl-2-oxazolidinones
AU Failla, L.; Massaroli, G. G.; Scuri, R.; Signorelli, G.
IT 4122-79-6 16719-00-9 90204-97-0 90950-33-7 91086-22-5
91086-23-6 91086-24-7 91087-27-3 91346-54-2 91824-07-6
92325-83-2 **92328-07-9** 92654-21-2 92861-89-7
93722-18-0 93722-19-1 93722-20-4 94065-90-4 94374-28-4
94462-20-1 95022-68-7 96059-01-7

IT **92328-07-9**
RN 92328-07-9 CAOLD
CN 2-Oxazolidinone, 5-[(4-methyl-1-piperazinyl)methyl]-5-[(5-nitrofurfurylidene)amino]- (7CI) (CA INDEX NAME)



L107 ANSWER 6 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA59:615b CAOLD
TI bicyclic homologs of piperazine - (III) **synthesis** of pharmacol. active 8-methyl-3,8-diazabicyclo[3.2.1]-octanes
AU Cignarella, Giorgio; Occelli, E.; Maffii, G.; Testa, E.
IT 1504-71-8 1507-92-2 1794-54-3 4370-81-4 7465-18-1
17740-50-0 34933-24-9 46810-47-3 50385-93-8 59436-67-8
63977-90-2 63977-91-3 63990-42-1 77502-62-6 90048-58-1
90049-31-3 91445-47-5 91445-55-5 93760-74-8 93864-20-1
94163-61-8 94163-62-9 94461-71-9 94462-08-5 95556-93-7
95556-94-8 97031-96-4 **98000-60-3** 98309-86-5
98801-79-7 100958-64-3 105067-93-4 106338-40-3 106338-41-4
106479-37-2
IT **98000-60-3**
RN 98000-60-3 CAOLD
CN Phthalimide, N-[(8-methyl-3,8-diazabicyclo[3.2.1]oct-3-yl)methyl]- (7CI) (CA INDEX NAME)



L107 ANSWER 7 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA56:1962b CAOLD
TI 1,2,4-oxadiazole - (IV) **synthesis** and pharmacol. properties of a series of substituted aminoalkyl-1,2,4-oxadiazoles
AU Palazzo, Giuseppe; Tavella, M.; Strani, G.; Silvestrini, B.
IT 879-57-2 1822-94-2 10560-64-2 22179-77-7 36957-30-9
40019-44-1 40312-16-1 49773-26-4 50737-32-1 51802-77-8
53919-74-7 57238-75-2 57238-76-3 89169-32-4 89169-33-5
89169-42-6 89169-50-6 89213-60-5 89213-61-6 89213-62-7
89213-65-0 89305-41-9 89305-43-1 89305-52-2 89305-54-4
89306-01-4 89620-26-8 90002-06-5 90030-71-0 90224-62-7
90272-90-5 90272-96-1 91066-23-8 91066-47-6 91430-24-9
91721-21-0 91721-36-7 91721-50-5 92286-42-5 92286-43-6
92294-66-1 92427-80-0 92434-98-5 92800-29-8 92819-89-1
93030-74-1 93048-81-8 93048-83-0 93335-40-1 94267-78-4

94626-69-4 94626-70-7 94627-01-7 94980-87-7 95373-35-6
95373-36-7 95494-33-0 95515-26-7 95591-27-8 95592-53-3
95707-28-1 95709-23-2 95844-44-3 95844-45-4 95983-36-1
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96535-19-2 96634-31-0 96716-07-3 96777-11-6 96877-26-8
96954-79-9 **97001-84-8** 97174-32-8 97192-53-5
97237-32-6 97238-06-7 97238-27-2 97238-67-0 97281-79-3
97285-29-5 97319-11-4 97319-69-2 97379-02-7 97407-45-9
97407-46-0 97407-47-1 97407-53-9 97407-54-0 97407-55-1
97438-58-9 97470-35-4 97496-12-3 97496-13-4 97497-39-7
97497-43-3 97497-49-9 97498-46-9 97593-89-0 **97598-01-1**
97616-91-6 97616-98-3 97617-01-1 97617-02-2 97617-03-3
97617-12-4 97617-13-5 97617-14-6 97723-79-0 97739-66-7
97739-68-9 97771-48-7 97786-43-1 97786-60-2 **97810-20-3**
97833-58-4 97833-59-5 97977-09-8 97977-10-1 98030-72-9
98172-89-5 98344-17-3 98344-43-5 98494-43-0 98562-64-2
98658-24-3 98693-01-7 **98780-08-6** 99005-50-2
99689-45-9 99711-05-4 100173-26-0 100174-28-5 100195-57-1
100195-58-2 100337-77-7 103192-77-4 105231-60-5 106571-94-2

IT **97001-84-8 97598-01-1 97810-20-3**
97833-58-4 98780-08-6

RN 97001-84-8 CAOLD
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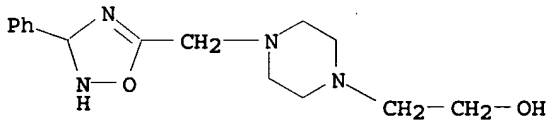
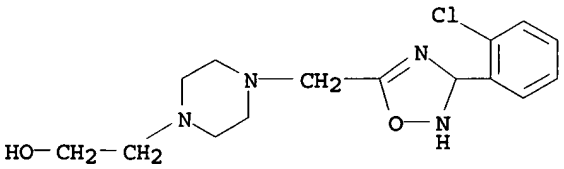
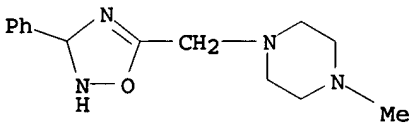


RN 97598-01-1 CAOLD
CN 1-Piperazineethanol, 4-[[3-(o-chlorophenyl)-Δ4-1,2,4-oxadiazolin-5-ylmethyl]- (7CI) (CA INDEX NAME)



RN 97810-20-3 CAOLD
CN Piperazine, 1-methyl-4-[(3-phenyl-Δ4-1,2,4-oxadiazolin-5-yl)methyl]- (7CI) (CA INDEX NAME)



RN 97833-58-4 CAOLD
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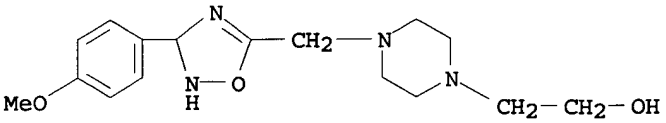
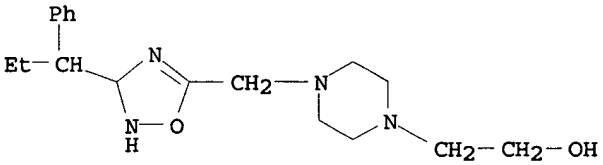


RN 98780-08-6 CAOLD
CN 1-Piperazineethanol, 4-[[3-(α-ethylbenzyl)-Δ4-1,2,4-oxadiazolin-5-yl]methyl]- (7CI) (CA INDEX NAME)



L107 ANSWER 8 OF 8 CAOLD COPYRIGHT 2006 ACS on STN
AN CA53:9198i CAOLD
TI **synthesis** and proof of structure of N-alkylated oxadiazolones
AU Caldwell, Henry C.; Seiwald, R. J.; Burckhalter, J. H.
IT 1199-02-6 2845-82-1 16219-60-6 41763-04-6 81404-39-9
108487-85-0 108800-25-5 108800-26-6 108903-18-0 109018-66-8
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117026-14-9 118927-11-0 120233-05-8
IT **109044-68-0 109963-24-8 109963-25-9**
RN 109044-68-0 CAOLD
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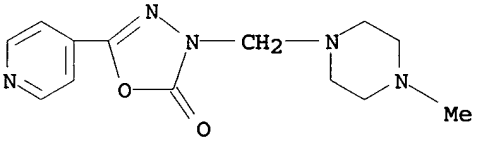

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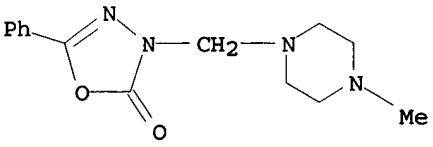

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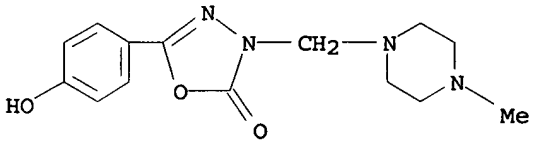

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